HOUSE OF LORDS

SESSION 1992–93

7th REPORT

SELECT COMMITTEE ON SCIENCE AND TECHNOLOGY

REGULATION OF THE UNITED KINGDOM BIOTECHNOLOGY INDUSTRY AND GLOBAL COMPETITIVENESS

VOLUME II—ORAL EVIDENCE
AND
WRITTEN EVIDENCE RECEIVED AFTER 30th APRIL 1993

Printed pursuant to the Order of the House of Lords *of 13th July 1993*

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MINUTES OF EVIDENCE
TAKEN BEFORE

THE SELECT COMMITTEE ON SCIENCE AND TECHNOLOGY

(SUB-COMMITTEE II REGULATION OF THE UK BIOTECHNOLOGY INDUSTRY AND GLOBAL COMPETITIVENESS)

Thursday 11 March 1993

HEALTH AND SAFETY EXECUTIVE

Mr A W Brown, Dr P H Buley, Dr S Smith,
Dr A Spalding and Dr A Cottam

DEPARTMENT OF THE ENVIRONMENT

Dr D J Fisk, Dr H Marquard and Dr I Gillespie

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MINUTES OF EVIDENCE

TAKEN BEFORE THE SELECT COMMITTEE ON SCIENCE AND TECHNOLOGY
SUB-COMMITTEE I

THURSDAY 11 MARCH 1993

Present:

Dainton, L.
Flowers, L.
Gregson, L.
Hilton of Eggardon, B.
Howie of Troon, L.
(Chairman)

Perry of Walton, L.
Platt of Writtle, B.
Renwick, L.
Soulsby of Swaffham Prior, L.
Walton of Detchant, L.
Whaddon, L.

Written Evidence from The Health and Safety Executive

Introduction

1. This submission is concerned chiefly with the legislation designed to protect the health and safety of human beings—both employees and members of the public—from risks arising from work activities in biotechnology. The Health and Safety Commission (HSC) is responsible for advice to Ministers on this legislation, and the Health and Safety Executive (HSE), as well as acting on behalf of the Commission, independently enforces it.

Health and Safety: the Regulatory Framework

2. On the whole the risks to human health and safety associated with biotechnology in the workplace are not singled out for special treatment in UK legislation. They are dealt with by a broad body of law which includes and is built upon the Health and Safety at Work Etc Act 1974 (HSWA). The HSWA itself imposes general duties on employers and the self-employed to protect employees and the public, so far as is reasonably practicable, against the risks created by their activities. Regulations made under it, and not specific to some other activity, also apply. In particular the Management of Health and Safety at Work Regulations 1992 develop the provisions of the HSWA and expressly require, among other things, an assessment of risk so that controls can be correctly chosen.

3. More immediately relevant to biotechnology are the Control of Substances Hazardous to Health Regulations 1988 (COSHH), which set out more detailed requirements for the control of risks arising from exposure to a wide class of substances including harmful micro-organisms. Many of the organisms involved in biotechnology, and the ones of greatest interest as regards health protection, are micro-organisms, and although few actually create a hazard to health they fall within the scope of COSHH if they do. HSC is about to issue consultative proposals to amend COSHH in order to implement EC directive 90/679/EEC, on the protection of workers against risks arising from exposure to biological agents. The amendments will extend the regulations to a slightly wider range of biological agents than before (it will include cell cultures and some parasites), elaborate some of the existing duties and add a small range of new ones. A significant addition will be a requirement to notify HSE of certain activities involving the more hazardous agents, though much of this is already in force under the Health and Safety (Dangerous Pathogens) Regulations 1981, which the proposed amendments will revoke.

4. Notwithstanding this body of law, what people usually have in mind when they speak about the regulation of biotechnology is the legislation dealing specifically with activities involving genetically modified organisms (GMOs). The remainder of this submission focusses on that legislation, just as it forms only a part of the whole regulatory framework, so the activities subject to it make up only a part of all that goes under the general heading of biotechnology. Most industrial applications still rely on organisms or biological systems that occur naturally or are adapted by traditional methods. This is true, for example, of the biological production of antibiotics and other pharmaceuticals, the production of enzymes as ingredients in food or cleaning agents, biological waste treatment, the many activities in agriculture and animal husbandry involving selective breeding, and ancient manufacturing processes such as brewing and chees making. The use of GMOs will undoubtedly grow, is potentially of great economic importance and is certainly where current interest lies, but for the moment most biotechnological activity is traditional and not subject to special regulation.

5. The legislation specific to GMOs is divided into two parts. The Genetically Modified Organisms (Contained Use) Regulations 1992 cover most activities in which GMOs are prevented from escaping into the environment, by physical or by physical combined with chemical or biological means. The Genetically Modified Organisms (Deliberate Release) Regulations 1992 in combination with the Environmental Protection Act 1990 cover the release of GMOs to the environment and the marketing of GMO products. Both sets of regulations are intended to protect the environment as well as human health, and a central feature of both is a procedure for notification and consent. The background to this legislation and its content are dealth with in more detail below.

Background to the GMO legislation

6. Regulatory controls on GMO activities are unusual in the health and safety field in that they originated with a caution voiced by scientific practitioners themselves, and have always been a precautionary response to conjectural risks. No historical record of mishap or empirical evidence of special risks associated with genetic modification has been assembled.

7. Fears were first expressed in America in the early 1970s, and in July 1974 a National Academy of Science study group published a seminal letter in the journal "Science" calling for a moratorium on certain GMO experiments. Among the envisaged possibilities causing alarm at that time were that a pathogenic bacterium modified to make it resistant to antibiotics (a property sometimes used as a "marker" to enable GMOs to be distinguished from other organisms) might escape and cause untreatable disease, or that organisms might be produced capable of transporting tumour inducing genetic material into the cells of human beings. Voluntary restraint was agreed, while the National Institutes of Health (NIH) set up a Recombinant DNA Advisory Committee and prepared guidelines for GMO laboratory work. Guidelines were published in 1976. Initially they were strict, but since then have gradually been relaxed as knowledge has developed.

8. Meanwhile scientific circles in Britain also moved quickly. The Ashby working party, set up by the Advisory Board for the Research Councils, examined the benefits and hazards of genetic modification work. In its January 1975 report the working party gave genetic modification techniques an "amber light", recommending that with rigorous safeguards they should continue to be used in view of their great potential benefits.

9. To take forward the Ashby work the government convened the Williams working party, which reported in August 1976. It drew up a code of practice for GM laboratory work and recommended the formation of a "Genetic Manipulation Advisory Group (GMAG)" to examine proposals for GMO work. It saw as one of the functions of GMAG the building up of a body of "case-law", against which to judge individual experiments. It proposed that regulations should be made under the Health and Safety at Work Act requiring submission of experimental proposals in advance so that GMAG could consider them. GMAG was set up in December 1976, and in 1984 became what is now HSC's Advisory Committee on Genetic Modification (ACGM). The Health and Safety (Genetic Manipulation) Regulations 1978 required notice to HSE and GMAG of "any activity involving genetic manipulation". They were replaced by the Genetic Manipulation Regulations 1989 which extended the notification duty to cover the use of GMOs and the release of GMOs to the environment, though a range of activities judged to be of low risk were subject only to inclusion in a retrospective list. The 1989 regulations remained in force until revoked on 1 February 1993 by the 1992 Contained Use Regulations. Being made under HSWA, both the 1978 and 1989 regulations were confined to the protection of human health.

10. Parallel developments took place in Europe. In 1983 the OECD Committee for Scientific and Technological Policy set up a Group of National Experts for Safety in Biotechnology, to examine the industrial and environmental applications of GMOs which were then beginning to appear as the technology moved out of the laboratory. It published its conclusions in 1986 in an influential document that has become known as the "Blue-Book". It set out and advocated the principles of "Good Industrial Large Scale Practice (GILSP)", based on the use of intrinsically low-risk organisms needing minimal containment, as well as providing guidelines for the containment of organisms too hazardous for GILSP safeguards to be sufficient. The Blue Book recorded the Group of National Experts' conclusion that there was "no scientific basis for specific legislation for the implementation of rDNA techniques and applications". However taking into account the broader concerns of member states the EC Commission began to prepare proposals for directives, drawing on the OECD work. These ultimately became directives 90/219/EEC and 90/220/EEC, adopted in April 1990, the first dealing with the contained use of GMOs and the second with release and marketing.

11. Both directives had the aim of protecting both human health and the environment. This meant that implementation in the UK involved both HSC/E and the Department of the Environment, and two principal parent statutes, the Health and Safety at Work Act and the Environmental Protection Act 1990. The Environmental Protection Act contains a section (Part VI) dealing specifically with GMOs, as recommended

by the Royal Commission on Environmental Pollution. The first consultative proposals for implementing legislation were issued jointly by HSC and DoE in October 1991. They were extensively revised in the light of the comments that were received and reissued in August 1992, in a form that became the basis of the current regulations. As outlined in paragraph 5 above the regulations follow the structure of the directives themselves, with two sets, one for contained use and one for release, each dealing with the protection of human health and the environment (and drawing on the European Communities Act 1972 in order to go beyond the limits of HSWA and EPA in that respect).

Main features of the GMO regulations

12. This submission concentrates on the 1992 Contained Use Regulations as it is these that are concerned most directly with human health protection, for which HSE is responsible. Organisms posing a more than an insignificant risk to human health would not be candidates for release (except in certain special circumstances of potentially high benefit, some vaccines and pharmaceuticals for example), and the focus of the deliberate release regulations is correspondingly on the protection of the environment. For these reasons HSE has taken the lead in the preparation and administration of the Contained Use Regulations, and DoE has led on release and marketing.

Contained Use

13. The Contained Use Regulations follow closely the structure and terms of the Contained Use Directive, going beyond it only in two respects. They continue current UK legislative practice in applying not only to micro-organisms but also to the human health risks associated with large organisms such as plants and animals, while the directive is confined to micro-organisms. And they provide for certain information on GMO work to be made available by means of a public register. The directive does deal with information disclosure but is silent as to the means.

14. A central requirement of the Contained Use Regulations is that a risk assessment is carried out before work begins, so that containment measures can be currently selected. A system of notification and consent is set up, based on a classification scheme for both the organism and the activity in which it is used. There are provisions for the preparation of emergency plans, the notification of accidents, and for the disclosure and retention of information. Fuller details of the regulations are set out at Annex 1. The Contained Use Directive which underlies them is at Annex 2, and the regulations themselves, with accompanying guidance published by HSE, are at Annex 3.

Deliberate release

15. The main features of the Environmental Protection Act and the 1992 Deliberate Release Regulations, in respect of the release and marketing of GMOs, are described in detail in separate evidence submitted to the Committee by DoE. They extend to a slightly wider range of GMOs than do the Contained Use Regulations, which exclude from their scope some low-hazard self-cloned organisms and the construction and use of somatic hybridoma cells. Provisions are included for the disclosure of information to the public but differ in some respects from those in the Contained Use Regulations, reflecting the greater significance of deliberate release to the public and the differences between contained use and release in the kind of protection that is needed for commercially sensitive information.

Administration and enforcement

16. The two sets of regulations are administered jointly by HSE and DoE, together with the Ministry for Agriculture, Fisheries and Food as regards matters affecting its area of responsibility, and the Welsh and Scottish Offices as regards environmental matters in their territories. The regulations themselves require in particular that a contained use consent is not granted by HSE without the agreement of the Secretary of State for the Environment (or Scotland or Wales) insofar as it relates to environmental protection, and a reciprocal procedure operates for release and marketing consents granted by the Secretary of State insofar as they relate to the protection of human health. These arrangements and others for coordination and cooperation are the subject of a Memorandum of Understanding between the departments involved.

17. All this legislation is enforced by HSE. For the Contained Use Regulations the powers used are those conferred by the Health and Safety at Work Act. For the release legislation the Secretary of State's enforcement functions under Part VI of the Environmental Protection Act have been delegated under an agency agreement to HSC, and thence to HSE. The agreement is to be reviewed in two or three years time to take account of the establishment of the planned Environment Agency. Inspection and enforcement are carried out by the team of specialist HSE inspectors, forming part of HSE's Technology and Health Sciences Division, which was already enforcing the 1989 regulations. It has six members, all qualified at least to degree level in relevant disciplines. All undergo a one year HSE training programme before joining the team, and undertake in post a further structured programme of training and professional development in biotechnology.

18. The broader legislation referred to at paragraphs 2 and 3 above, in most activities not involving GMOs, is enforced by HSE's general factory and agricultural inspectorate.

Burdens and competitiveness

19. The questions that have been raised about the burdens and the effects on competitiveness of UK health and safety legislation as applied to biotechnology have mainly been about the law specifically dealing with GMOs. It should be borne in mind however that, as noted at paragraph 4 above, this is a small part of the regulatory framework and applies to a small proportion of biotechnological activity. The substantive safeguards that are needed, those that involve expensive engineering and systems of work, are required in any case by more general legislation such as the Health and Safety at Work Act and the Control of Substances Hazardous to Health Regulations. The additional measures required by the GMO legislation must be seen against this background. Even so, although they will rarely bar an activity by the placing of conditions on the work itself, they do impose some burden. There are administrative costs in the preparation of notification documents and applications for consent, both directly incurred and transferred to the notifier in the fees charged, and the scheduling of work will be affected by the need to go through clearance procedures before a start can be made.

Particular competitiveness issues

20. Three particular issues have arisen in early reaction to the Contained Use Regulations which warrant explanation. The first is whether the criteria used to classify organisms for the purposes of the regulations are unnecessarily burdensome by being ambiguous, or worse, wrongly set. The second is the same point but in relation to the criteria used to classify activities. The third is whether some organisations will face high costs by being required to make multiple notifications. They are examined in paragraphs 21–23 below.

21. The criteria used to divide micro-organisms into lower and higher hazard groups (referred to in the regulations as Group I and Group II) are taken from the contained use directive and a supporting CEC decision (91/448) which sets out classification guidelines. Broadly speaking they are intended to distinguish between organisms that are pathogenic to humans, animals or plants and those that are not. They do this by applying multiple tests to the host organism, the genetic material to be inserted into it, and the means of insertion. They are based on criteria developed earlier by OECD and widely accepted as a basis for classifying organisms. Flexibility and qualifications are built in, to allow for the subtleties of hazard assessment in this field, and this does mean that there will be marginal cases needing careful interpretation. Some reasoning and judgment in the use of the criteria is unavoidable because of the scientific complexity of the assessment and, sometimes, uncertainty about the organisms and genetic material involved. There is a trade-off between flexibility and lack of ambiguity, both wanted by practitioners. To a degree difficulties can best be dealt with by refining guidance in the light of experience. But none of this is to say that a consensus will not emerge pointing to an adjustment of the threshold set by the present criteria.

22. The criteria for classifying activities are also taken from the contained use directive, with some elaboration to relate what is meant by "small-scale" to the activity under consideration. There are two conditions which an activity must satisfy to be placed in the less strictly regulated group (Type A), one of purpose and one of scale. The purpose must be teaching, research, development *or* an non-industrial or non-commercial purpose. Most activities in question are research or development. The "commercial" test need not normally be applied, though it is the one that has worried commentators most. The scale must be "small", but what counts as small depends on the process and facility. It must be possible to contain a spill if primary containment fails. Standard laboratory decontamination must be sufficient and easily undertaken (if, say, a tanker of biocide is needed the scale is by definition not "small"). Different activities may satisfy these tests at widely varying volumes. The contained use directive gives an indicative figure of 10 litres but this is unhelpful in practice. Even so most commentators are relatively happy to subject the scale criterion to common sense reasoning case by case. The shortcoming of the activity criteria, if there is one, is not so much ambiguity as that the test of purpose is not related to risk, though this may underclassify, say, a research activity, as well as overclassifying some industrial production.

23. The third point mentioned at paragraph 20 above is the suggestion that the regulations will unduly burden organisations that carry out large numbers of individual GMO activities by requiring a correspondingly large number of separate notifications and fees. This is a perceived difficulty mainly in academic institutions which may carry out large numbers of experiments using pathogenic organisms. Many of these were notifiable under the 1989 regulations, though not subject to a fee. (Type A activities using Group I organisms are not notifiable separately or in advance). The problem is largely solved by the regulations themselves, which allow a group of activities making up a connected programme of work to be collected in a single notification. It will usually be possible in this way to reduce the number of notifications required. Generally the number of discrete programmes in a given institution will be limited by the number and feasible range of interests of the supervisory academic staff. By their nature, large-scale or industrial activities either involve few discrete processes or are connected by the commercial ends of the company, and do not give rise

to multiple notifications. Once a set of activities has been notified, the regulations allow information about changes and developments in it to be submitted without being counted as a new notification liable to a fee.

24. Other aspects of the regulations and their application in which efforts have been made to avoid undue pressure on duty holders are:

— the arrangements for enforcement; and

— the provisions for information disclosure.

25. Unified enforcement by HSE means that organisations will see a single, coherent enforcement body familiar with their activities and providing continuity with the past. Dual inspection, with the risk of conflicting advice being given for different purposes, will be avoided. The flexibility in the regulations allow for them to be interpreted by expert inspectors in a pragmatic way, and for advice to be given on best practices.

26. Information disclosure more than any other single issue alarmed commentators during the consultation exercise on the proposed regulations because of the threat to competitiveness and the patentability of inventions. The regulations contain a carefully constructed compromise which has reassured industry that competitiveness and intellectual property rights will have the protection they need, while being able to meet any public demand for information as far as possible.

Burdens and benefits

27. The question remains whether the genuine burdens imposed by the regulations are justified (aside, of course, from the fact that they stem from requirements at present contained in EC directives which we are bound to implement). As indicated above, the received view about the risks to human health associated with GMOs has become much more sanguine since the 1970s, a change signified, for example, by the gradual relaxation of the American NIH guidelines. By 1982 GMAG was able to say in its third report: "...it has become apparent that the hazards specifically attributable to genetic manipulation of micro-organisms are, if they exist at all, far less than was conjectured when the Group was set up..." The conclusion of the OECD Group of National Experts that GMO legislation was not called for has been noted. The trend has continued, and it is now accepted that most GMO work entails little danger beyond that of conventional activity with biological agents.

28. There are several reasons for this. One is the accumulating historical record of GMO experiments and other activities without the creation of any novel hazard (20,000 individual activities have now been carried out since notification began with the 1978 regulations). More compelling is that studies designed to test the hypothesis that a host organism can acquire unexpected properties have failed to demonstrate them. To take one of the early fears referred to earlier—that a pathogenic micro-organism might acquire drug resistant properties and cause untreatable disease—it is now apparent that the combination of events that would have to take place for that to happen is extremely improbable. Combined with this a growing confidence that the organisms used for GMO experiments can be selected so that they are unable to survive except in the special environment of the experiment or process in which they are used. It is still possible to envisage an act of evil genius, but there is nothing unique to biotechnology in that, and it is probably easier to wreak havoc by more conventional means.

29. The 1989 Genetic Manipulation Regulations contained graded notification requirements which reflected this developing assessment. The Contained Use Regulations, in implementing the Contained Use Directive, have reverted to a stricter regime (in particular by requiring notification in advance of a range of low-risk industrial activities previously subject only to submission of a retrospective count), which the argument above would suggest is more than is necessary for the protection of human health. It is important to recall, however, that one of the purposes of both the directive and the regulations is the protection of the environment, and here, although the hazards are still conjectural, there is as yet less certainty. Two envisaged environmental effects not yet ruled out are the transfer of undesirable traits to indigenous populations (for example the transfer of herbicide resistance from a transgenic plant to a weedy relative), and the displacement of an indigenous population by a transgenic intruder. Although it is reasonable to suppose that assessments of the risk will develop as have those in respect of human health, and that control will not be difficult, as long as the two purposes are combined in the legislation it has to reflect the greater doubt.

30. A further justification and benefit for regulation of a demonstrably thorough kind stems from public perception and its effect on the application of biotechnology. There is still a good deal of understandable public disquiet. Fear of the production of a rogue organism or ecological disturbance, sometimes fanned by melodramatic media treatment or conflated with moral reservation about interference with the foundations of life, and not offset by reports of beneficial applications, leads to a demand for strict regulation pushed to the point of prohibition. This is a powerful force with the capacity to inhibit development of the technology

in ways disproportionate to a rational assessment of the risk. The reassurance given by transparently effective regulation helps to moderate it (see also paragraphs 48 and 49 below).

QUESTIONS PUT BY THE SELECT COMMITTEE

What is your interest in biotechnology?

31. Under the functions conferred on it by HSWA the Health and Safety Commission is responsible to the Secretary of State for Employment, and to other Secretaries of State as appropriate, for the administration of the Act and the regulations made under it, including the ones which are the subject of this note. It keeps under review the adequacy of current legislation and submits to Goverment proposals for new or revised regulations when they are called for. It delegates many of its functions to HSE as its main operational arm, though in the day to day enforcement of the Act and regulations the Executive is independent of the Commission. As mentioned above, HSE enforces all the current legislation implementing the two EC directives on GMO activities.

32. HSE and DoE are joint competent authorities for the purposes of the GMO directives, and HSE officials take part in discussions and negotations in EC committees, as well as in other international groups convened by OECD and other bodies.

How and why is biotechnology important to UK industry? What future prospects and opportunities does the technology offer?

33. From an economic point of view these questions will be fully answered by others, but HSE is aware that biotechnology has huge potential in manufacturing, medicine and other fields, and that it is a nascent technology the development of which in the UK could be damage if it is trammelled by inappropriate regulation. The more direct effects on HSE are likely to be a growing incorporation of biotechnological processes into routine industrial and agricultural activity, with the corresponding development of a body of accepted health and safety standards and practices, and possibly the replacement of some traditional, relatively "dirty", industrial processes by safer ones making use of the new technology. This assimilation of the new technology into the mainstream would be accompanied by some transfer of inspection and enforcement duties to HSE's general factory and agricultural inspectorate, to the extent that the training and expertise of its members were sufficient, with the specialist team (paragraph 17 above) retaining responsibility for activity whcih had not become so normalised and available to give expert advice in cases of difficulty.

Which developments in biotechnology raise issues of safety and how should they be addressed?

34. This question is considered above in relation to activity involving GMOs, though it should be recalled that there are many other biotechnological activities in which GMOs are not used, and which are controlled by general health and safety legislation. For GMOs a framework of regulation now exists based on the two EC directives, and the expressed intention of HSC/E is to monitor and evaluate it in operation and seek amendment of the directives as necessary in the light of experience. Experience so far suggests that such amendment is likely to be in the direction of a relaxation of controls, and towards assimilation of GMO regulation into more general law.

Should biotechnology be regulated by an industry-specific regime?

35. Most risks to health and safety are not confined to a particular industry, and the control measures applied to them are universal. For that reason legislation is more appropriately structured by risk or risk agent, and with few exceptions that is the way that it has been developed in recent years. Regulations deal, for example, with the risks associated with noise, electricity, manual handling, or toxic substances, wherever they occur. This makes for a simpler legislative structure discriminating according to the factors that actually cause harm, and applying consistent standards across the whole field of industry without gaps.

36. The same reasoning applies to biotechnology, which is not really an "industry" at all. It is a broad group of enabling technologies and techniques with wide and diverse applications in a number of fields. Following current legislative practice, we should want to see whether there are categories of risk in any of these applications that call for control. What is unusual here is that one group of techniques, those involving genetic modification, give rise to particular concerns that have led to regulation by technique family. But there is no one risk or range of risks associated with this family, and as a result the legislation does not so much directly control risk as seek to make sure that attention is given to the possibility that there might be one. This

has been a justifiable precautionary approach which it may or may not be resonable to relax, but the concept of "an industry specific regime" is not really applicable.

From a technical point of view, is horizontal regulation better than vertical regulation? Should regulation evolve from a horizontal to a vertical approach in each industrial or environmental application?

37. This question arises principally in connection with the clearance of products for the market. For workplace activity the remarks made above on industry-based legislation apply a fortiori to the idea of regulation by product. If there are risks they are not product specific at this level, and to regulate on that basis would require a plethora of sets of regulations that could never keep up with developments.

38. For the marketing of products, the answer to the question depends upon whether the product in question is one that needs scrutiny and clearance anyway, because of its essential properties and application—medicines and pesticides are obvious examples. In these cases it is sensible and efficient to incorporate into the clearance procedure any particular scrutiny needed to take account of a product's biotechnological origins, so as to avoid dual process by both vertical and horizontal routes. The deliberate release directive makes provision for this at Community level where there are product-based directives, and it is current government policy that the same substitution should be embodied in UK law. Several product directives are in the pipeline, and it is likely that many biotechnology products will be covered by them in the coming years.

39. For products that are not and are not to be vertically regulated for other reasons, there is no advantage in treating them that way solely in virtue of their link with biotechnology. To do so, as in the case of workplace regulation, would lead to a large number of separate pieces of legislation and clearance procedures discriminating on a false basis and struggling to keep pace with new products. A suggestion that is sometimes made—that legislation should evolve uniformly towards the vertical because what matters is always the properties of a product and not the method by which it is made—has some force but begs the question, which is precisely whether there is something about biotechnology that does give grounds for special attention. Moreover it is self defeating. For all the products that would not otherwise be vertically regulated the introduction of such legislation would imply a special biotechnological aspect, but that in itself would justify horizontal treatment.

How do current regulations compare with those of other competitor countries in Europe, the far east and the USA?

Europe

40. In Europe a more or less uniform system, and level playing field, is being established by the two GMO directives and the activities of the EC Commission in applying them. Implementation so far, however, is patchy, with several member states still relying on old systems of guidance or existing legislation drafted to deal with "traditional" products.

41. Apart from the UK (except for Northern Ireland) the following member states had implemented the directives at the end of 1992:

(a) Germany. Implementation was by means of the 1990 Gene Law, but it has been judged insufficient by the EC Commission and infraction proceedings have been started. At the same time the regime has been found to be harsh and restrictive by German industry and academic institutions. Some commercial operations are subject to public hearings which cause restriction and delay. Administration is by the separate state governments, which has led to wide variations in approach. Responding to all these objections the government has agreed that the legislation should be amended;

(b) France. Primary legislation was introduced in 1992, putting on a statutory footing an existing system of scrutiny by two committees based in the ministries of agriculture and research and technology, and supplemented by the application of standards issued by the French Standards Institution. Decrees necessary fully to implement the directives are still being prepared;

(c) Denmark. Legislation to regulate GMO work was introduced in 1986, based on a system of approval and consent. It has been amended to bring it into line with the directives but this has meant a relaxation rather than a tightening of controls and the Danish legislation is still more burdensome for "Good Industrial Large Scale Practice (GILSP)" users than the contained use directive demands, and goes beyond the directive in a number of other areas;

(d) Netherlands. Implementation has been by amendment of existing legislation dealing with chemical substances.

42. It is difficult at this stage to predict whether competitive irregularities will be introduced within the framework set by the directives, though Germany and Denmark have already shown how a political and social climate can lead to tougher regulation than is implied by community rules. One area where variation is possible is in the fees charged by competent authorities. Both France and Denmark charge significantly higher

fees than does the UK for example. (Current UK fees for a contained use notification range from £100 to £270 depending on the amount of scrutiny and processing needed).

43. Under the 1991 agreement between the EC and EFTA which led to the formation of the European Economic Area the EFTA nations—Iceland, Norway, Sweden, Switzerland, Austria, Liechtenstein and Finland—were due to implement EC legislation including environmental and internal market measures during the mid 1990s. Meanwhile, existing systems of control have made use of American guidelines and the OECD Blue-Book. There is advisory committee review in Finland and Switzerland. Norway controls the release of GMOs under a range of existing sectoral legislation. Austria has established a parliamentary commission to determine its regulatory policy for work with GMOs which was due to report in late 1992.

Japan

44. Japan's oversight of GMO work is within a framework of guidance rather than regulation. As in the case of the American NIH guidelines the Japanese guidance has been relaxed in a series of revisions since its first issue in 1979. There is an extensive system of voluntary review by industry and health departments.

USA

45. Contained use in the USA is largely controlled by the NIH guidelines referred to above, rather than by specific regulation. Federally funded projects have to be approved by a scrutiny panel on the basis of the guidelines, but other proposers generally submit to the same procedure voluntarily. Since 1987 NIH approval has been required for any project involving human gene therapy.

46. The control of the release of GMOs is complex, involving several different agencies and pieces of existing product-based review schemes. The Food and Drugs Administration operates the Federal Food, Drug and Cosmetic Act, which regulates foods, food additives, pharmaceuticals, cosmetics and medical devices. The US Department of Agriculture, through the Federal Plant Pest Act, Plant Quarantine Act and Virus-Serum-Toxin Act, deals with veterinary vaccines and with plants and micro-organisms that could be plant pests. The Environmental Protection Agency, through the Federal Insecticide, Fungicide and Rodenticide Act and the Toxic Substances Control Act, deals with pesticide products and substances, including micro-organisms, not regulated elsewhere. A variety of notification and consent procedures is operated by these agencies. The regulation of biotechnology is currently under review at federal level, and the effect of the 1993 change of administration is not yet clear.

What are the consequences, or likely consequences, of the regulatory regime on competitiveness of the UK industry, in particular as regards research, product development, investment, location, sales and marketing? Is there a danger that the present regulatory regime will prevent the exploitation by British industry of research conducted in the UK science base?

47. These questions are largely for others to answer, but HSE is conscious of the need for regulation that does not damage competitiveness if that can be avoided, and through the extensive consultative procedures required by HSWA can become aware of industry concerns. As a result the present regulations, insofar as they follow the requirements of the directives closely, should not put UK industry at a disadvantage at least with respect to other EC member states. As explained, special efforts were made in the area of information disclosure to make sure that this was so. In the administration of the regulations HSE does its utmost to make requirements and procedures simple and transparent to duty-holders, so that they are not burdened by unnecessary complexity. The regulatory regime has not prevented the exploitation of research conducted in the UK science base so far (witness the twenty thousand notified activities since 1978) and there is no reason why the future should be different. It seems likely that the economic and business climate will be much more influential.

How best can issues of public acceptance be addressed?

48. This is a difficult problem because of the complex of fears and antipathetic reactions, some emotionally charged and linked with powerful ethical and religious convictions, elicited by genetic modification. It is often suggested, especially by practitioners, that the answer lies in the provision of information, on the grounds that if people were better informed they would see that their doubts were unfounded. There is evidence however that this does not work, and that all but the most meticulously open-minded fit new information into an existing belief system and use it to reinforce those beliefs.

49. It may be that the promoters of biotechnology would do better gradually to encourage a familiarity with the technology and its benefits by making sure that advances , especially in fields of particular public interest like disease treatment, are well publicised. Meanwhile a system of regulation and control which is conspicuously thorough enough to reassure, and a clear willingness on the part of industry to abide by it, will be important. It is necessary, certainly form HSC/E's point of view, that the arguments about health and safety are properly distinguished from those on ethical and other grounds. HSC/E will aim to ensure that they

are, to provide as clear a picture as possible of the means by which public health and safety are to be secured, and to contribute to an informed public debate on that subject.

February 1993

ANNEX 1

The Genetically Modified Organisms (Contained Use) Regulations 1992

Application of the regulations

1. The Contained Use Regulations define the genetic modification of an organism broadly as "the altering of the genetic material in that organism by a way that does not occur naturally by mating or natural recombination or both", and go on to give examples of techniques which definitely do count, some that do not, and some that count but are excluded from the regulations anyway. The last category includes mutagenesis, cell fusion of plant cells where traditional breeding could have produced the same result, and self-cloning of certain less hazardous organisms, provided in each case that GMOs are not involved as recipient or parental organisms.

2. An activity counts as contained use if there are physical barriers, possibly supplemented by chemical or biological ones, limiting contact between the organism and the population and environment. EC Competent Authorities have agreed, however, that waste streams containing Group I organisms (see below) are however treated as not breaching containment, on the grounds that they have inbuilt biological barriers limiting their survivability in the environment.

3. The regulations cannot cover the *environmental* risks arising from the contained use of non-micro-organisms, whole plants or animals for example. This is because they are made under the Health and Safety at Work Etc Act 1974 and the European Communities Act 1972, the first limited to human health protection and the second to the requirements of the directive, the directive in turn being limited to micro-organisms. Similarly limiting the regulations would have meant leaving out a group of organisms which may be environmentally important, and one hitherto covered in respect of human health by the 1989 regulations. The gap has been closed by applying section 108(1)(a) of the Environmental Protection Act to these risks, requiring an environmental assessment to be made, and the effect is much the same as though the contained use regulations applied uniformly.

Categorisation of organisms and activities

4. The application of some of the main requirements of the regulations is partly governed by a classification scheme, drawn from the directive, which allocates genetically modified micro-organisms (GMMs) to two classes, genetically modified non-micro-organisms to two of their own, and activities involving GMOs to a further two. The combinations of organism type and activity type determine how the regulations apply.

5. GMMs are divided into what are called Group I and Group II according, broadly speaking, to their likely pathogenicity or ability to harm the environment. The regulations set down a range of criteria which must be satisfied before a GMM can be classified in the less hazardous Group I, covering the recipient or parental organism, the vector, the insert, and the final GMM itself. A point to note is that a pathogenic parental strain may be sufficient to place a GMM in Group II. If, however, the GMM is also a biological agent within the meaning of the biological agents directive, and the effect of the modification has been to reduce its pathogenicity sufficiently, it may appear in the lowest of the different set of four hazard groups used for biological agents. The two classification schemes are independent, and this is one illustration of the difference.

6. Non-micro-organisms are simpler, and are divided into those which are as safe in the containment facility as the parental organism and those which are not.

7. Activities involving genetic modification are classified as Type A or Type B depending on their scale and purpose. Type A activities are generally small scale, and are for teaching, research, development, non-commercial or non-industrial purposes—typically laboratory work. Research and development work carried out in the laboratory of a commercial firm for the purpose of creating a process for future industrial or commercial exploitation is counted in this category. Type B activities are generally larger scale or repetitive industrial processes producing a product, either for marketing or use as a raw material.

Risk assessment

8. A key requirement of the regulations is that anyone carrying out genetic modification work should make an assessment of the risk that it presents to human health and to the environment. Some of the other legislation applying to GMO work also calls for risk assessment, the Control of Substances Hazardous to Health Regulations and the Management of Health and Safety at Work Regulations in particular, but the common elements of these assessments need not be repeated.

9. The GMO assessment concentrates on the organism and its effects. It is to some extent structured by the regulations, which make the classification of the organism and the setting of containment level two of the assessment's principal purposes, and guide the assessor by setting out a detailed range of factors to be taken

into account. The regulations also provide for the approval of a risk assessment method by the Health and Safety Executive, and make obligatory the use of any method so approved. The intention here is to follow the precedent set by the 1989 regulations and approve the method contained in the guidance on risk assessment issued by ACGM, which has been updated to serve this new purpose and to take account of environmental risks.

Notification and consent

10. It is mainly in their requirements for notification that the contained use regulations carry on from the 1989 regulations. Anyone intending to carry out activities involving genetic modification for the first time must notify HSE. After that, individual activities must also be notified, one by one except for Type A operations involving only Group I micro-organisms or the lower hazard category of non-micro-organisms, which require only an annual retrospective count, and connected programmes of work, which can be treated as though they were single activities. The new regulations go further than the 1989 ones here, in that individual Group I Type B activities, which includes those formerly treated as falling under the heading of "good large scale practice", are now separately notifiable.

11. Who should do the notifying, and whether a particular organisation counts as one centre or several, depends upon the organisation itself. It is has an integrated management structure and system of control for the work, and a single safety committee, then it is likely to count as one centre. If it divides into autonomous departments with separate committees it will make itself willy-nilly into more than one and each will have to notify the work it controls. (The regulations require that a genetic modification safety committee should be set up at each centre, with the specific function of advising on the risk assessments that are made.)

12. Two kinds of work may not go ahead until HSE has assessed the notification and given its consent: first time activities involving Group II micro-organisms, and subsequent individual activities of Type B involving Group II micro-organisms. Other activities may be started within a specified time after notification is made provided that HSE has not objected in the meantime. The regulations spell out in detail the information that has to be provided with a notification—it depends to some extent on the categories of organism and activity involved—and it will be carefully examined by HSE experts and others while consent or possible objection is being considered. The Department of the Environment (and other interested departments) will look at the environmental aspects, and in some cases the information will be submitted to the members of ACGM for their view.

Information disclosure

13. The regulations follow the contained use directive closely in making provision for the disclosure of information about GMO activity to the public. They distinguish between competitiveness on the one hand and intellectual property rights on the other. Except for some specified items, including a description of the organism and an evaluation of its effects on human health and the environment, notifiers may ask that the information they provide should be kept confidential on competitiveness grounds. If the case they make is strong enough HSE will do so. Notifiers may argue in addition that the items which cannot be withheld on competitiveness grounds should nevertheless be kept confidential because disclosure would damage intellectual property rights, which include the important matter of patentability. What is left over will be disclosable, and the information subject to an intellectual property rights claim but not withheld on that basis will be placed on a public register.

14. In making decisions about disclosure HSE is required to consult notifiers and will discuss with them how information may be structured to achieve the best compromise. A notifier is always free to withdraw a notification and if that is done no further disclosure will take place. The names of individuals working in genetic modification will not be revealed.

Safety, hygiene and containment

15. For work with Group I micro-organisms the regulations require the principles of good microbiological practice to be followed, and list some specific measures that must be taken for the control of exposure to GMOs, including the preferential use of engineering controls as opposed to personal protective equipment. The same measures have to be taken as far as they are applicable for non-micro-organisms. Additional rules are laid down governing the choice of containment measures for work involving Group II micro-organisms.

For Type B operations the levels and corresponding measures are set out in the regulations themselves, and correspond largely to the OECD Blue-Book system for large scale operations. For Type A operations provision is made for HSE to approve a method of determining containment measures, and the approved method has been based on establishment ACGM guidance.

Emergency plans and accident notification

16. An emergency plan must be prepared if it is reasonably foreseeable that an accident could endanger people outside the premises where the work is done or damage the environment. "Accident" is defined as an incident involving a significant and unintended release of GMOs presenting an immediate or delayed hazard. In practice the duty is likely to be largely confined to Type B operations involving Group II micro-organisms. Accidents must be reported to HSE, which in turn has a duty to inform the EC Commission about them.

Examination of witnesses

Mr A W Brown, CB, Head of Health Policy Division, Dr P H Buley, formerly Head of Branch, Health Policy Division, responsible for GM Regulations, Dr S N Smith, Health Policy Division, dealing with policy and administration of the GM Regulations, Dr A Spalding, Scientific Policy Unit, dealing with GM Regulations, and Dr A N Cottam, Enforcement Team in Health and Safety Executive's Technology and Health Sciences Division, Health and Safety Executive, called in and examined.

Chairman

1. May I welcome you to our first meeting and thank you very much for your written evidence, which was very full. Would you first, Mr Brown, kindly introduce yourself and your colleagues, say just a brief word about what they do and then, if there is anything by way of an opening statement that you would like to make, please make it?

(*Mr Brown*) Thank you very much, my Lord Chairman. It is a privilege to be called into this arena. If I may introduce my team, Dr Alison Spalding heads the scientific policy unit in the Health Policy Division, Dr Stuart Smith is charged essentially with the preparation, formulation and implementation of the regulatory system under the GMO regulations, Dr Andrew Cottam heads the inspection team, that is, the enforcement team that inspects premises out in the field and Dr Buley until recenlty headed the branch that is responsible for the GMO regulations. I am head of the division and, as you would expect of the head of division, my Lord Chairman, my expertise is thin in detail so I shall rely heavily, if it suits you, on my colleagues.

2. Is there anything that you want to say in general to begin with, Mr Brown?

(*Mr Brown*) My Lord Chairman, there is no general statement that I wanted to make. One point that our evidence might have brought out a little more strongly, I think, is the extent to which we have consulted very widely in the preparation of both sets of GMO regulations, not only within the formal committee structures that exist. Very large numbers of interested parties have also had the opportunity to contribute to the process of development. Indeed, the first attempt at a regulatory structure proved unsuccessful and we went round for a second bite of consultations. That leads me to make the more general point about the Health and Safety Executive's operation, which is that we do proceed in all our regulation making and standard setting activities on the basis of very extensive consultation with all the interests involved. That, of course, is partly implicit in the structure of the Health and Safety Commission itself, which is tripartite. That point having been said, my Lord Chairman, I think that we have said to you what we need to in the evidence that we have put before you and we should like now to seek to answer your questions.

3. As far as the formulation of the regulations is concerned is your department the lead department, Mr Brown?

(*Mr Brown*) On the formulation of regulations in this field, my Lord Chairman, we should expect where human health considerations were the prime issue to be looked to by the government—the secretary of state—to be the authoritative source for advice. In so far as the regulations impact on the environment then clearly the Department of the Environment are in the lead and we might or might not be brought in. In this area, of course, my Lord Chairman, the two issues are often inextricably bound up and therefore the result effectively is a joint lead role.

4. Your procedure presumbly is one of considerable consultation with other departments, one assumes with the authorities in Europe and with industry?

(*Mr Brown*) Yes, all of those, my Lord Chairman, and extensively so.

5. Do you get a good deal of support from industry in the formation of these regulations?

(*Mr Brown*) Yes, both in the sense that large numbers of comments came to us from industry, and not only from industry but, of course, from the academic world, who have a very profound interest here, and in the sense that we have had a number of constructive meetings with groups so that we have consultation both formally and informally and through the provision of comments on the consultative papers.

6. Is it your impression that industry is generally favourable towards the regulations that you have devised?

(*Mr Brown*) Our general impression is that after the end of the second round of consultations there was a general feeling that what had come out, given

[Chairman *contd.*]

always the fact that we were bound to implement the EC directives, made a fair amount of sense. However, that is not to say that every representative spokesman of industry was delighted to have a quite rigorous regime of regulation; it would be idle to pretend that. Given the fact that the European Community had decided with the agreement of all the Member States that legislation in this field was necessary, I think that it is fair to say—and I will ask Dr Smith and Dr Buley for their more immediate comments on their experience with the consultations—that the general mood was that we had produced something that was workable.

(*Dr Smith*) Yes, I think that that is right, my Lord Chairman. Since the regulations came into force there have naturally enough been one or two points of difficulty, principally on the application of classification criteria and on the operation of the notification scheme and, of course, now day to day points of interpretation arise inevitably in marginal cases. However, given that we had the directive to implement, the reaction of industry finally as it was presented to us was one of, I think, pleased relief that we had produced a very workable way of implementing the directives. That was particularly true on the matter of information disclosure, which was of great interest to industry and on which we have had a lot of discussion and on which we struggled hard to produce a workable compromise.

7. I know that it is early days in our enquiry so far, but we have formed an informal impression that industry did not really care for the regulatory regime which prevails. Do you think that we are mistaken in that?

(*Dr Buley*) Perhaps it is more correct to say that industry is not entirely happy with the two directives, my Lord Chairman. I think that they are reasonably satisfied that we have implemented the directives as best as can be done, but they have made no secret of the fact that they would like a more flexible regime if possible, and I think that they are hoping in due course the directives themselves will change. I think it is clear from our evidence that the whole history of regulation in this field is one of a very precautionary approach which over time can then be relaxed, and we envisage that this may well continue. As with all European directives, my Lord Chairman, there is a provision in both the directives for technical amendments to be made and the directives themselves can, of course, also be reopened, although that is more difficult. We envisage in this field that this is likely to happen but the European Commission will clearly first of all want to be satisfied that the directives are implemented in Member States.

8. Am I right in supposing therefore that industry to some extent does not really like what you are obliged to do but is fairly happy with the way that you are doing it?

(*Dr Buley*) I think that that would be a fair summary, yes, my Lord Chairman.

(*Dr Smith*) It is probably worth adding, my Lord Chairman, that there is not really a univocal response on this. While it is obviously true to say that in general industry would prefer not to be trammelled by regulation a good section of industry recognises that in this field, which is one where there is a good deal of public concern, the existence of a transparent regulatory regime which is seen to be precautionary can have a great many advantages.

Lord Gregson

9. One of the fears that have been expressed to us by industry is the level playing field problem because whereas, as usual, we will apply the directives fairly assiduously in this country, other countries in Europe will not and are not. How do you see yourself monitoring the United Kingdom situation with industry? One gets the impression that other countries in Europe gayly pass the necessary legislation and then stick it in a pigeon hole somewhere.

(*Dr Cottam*) My Lord Chairman, certainly within the United Kingdom one of the main mechanisms for monitoring implementation is through our inspection activities, and it would perhaps be useful if I were to explain how we approach that in the United Kingdom as opposed to the rest of the European Community. Within the United Kingdom responsibility for the inspection of GMO work rests with a small group of specialists who have been recruited because of their knowledge and experience of the industry. This approach has in fact been acknowledged by the industry itself to have the benefit of ensuring that the regulators have an in depth understanding of the biotechnology and its applications as well as ensuring both pragmaticism in interpretation of the legislation and a consistency in approach. It is true to say, I think, that in the rest of the European Community inspection is carried out by national labour inspectorates, who have a general responsibility for inspection of work places. It has been argued, however, that this can lead to a legalistic approach to compliance with the letter of the law because of a lack of understanding of the technology. Because of the differences in legal framework and hence approaches to inspection between Member States we recognise that we need to ensure that information on enforcement is exchanged. This can be done through the regular meetings of the competent authorities for the two directives. In conclusion, my Lord Chairman, I think what I should say is that the important point is to ensure consistency in compliance rather than inspection, and that can only be achieved when all the Member States have implemented the directives.

10. That would be the first time ever if they did, would it not?

(*Dr Buley*) Strangely enough though, my Lord Chairman, in this particular field unlike some other fields I think that we can say with all truth that some countries in fact are stricter than we are—particularly the German regime, I believe, and the Danish one—so that your general point is less true in this field.

11. What they complain about is the countries that do not, not the countries that do.

(*Mr Brown*) I think that Dr Spalding can tell us to what extent there is development in other countries.

(*Dr Spalding*) My Lord Chairman, the Danish have implemented the directive in a very strict

[Lord Gregson *contd.*]

manner and they have gone much further than the contained use directive. Germany again has implemented in a rather strict manner, about which their industry is unhappy. France is in the process of implementing it. We have not seen the final version yet, so it is difficult to say how strict they will be, but we gather that it will be very similar to the United Kingdom situation. I am not sure what other countries have implemented fully, in fact—yes, the Netherlands have also.

Lord Whaddon

12. Bearing in mind the two different approaches that this country and some continental countries have, have you come across any actual examples of instances where the regulations have not been applied as you would wish them to be?

(*Mr Brown*) It is very early days, of course, my Lord Chairman. The regulations have been in force—and in most countries, of course, they are not even in force now—in the United Kingdom only a matter of weeks literally, so it is really rather too early. I do not know whether Andrew Cottam can say from his experience of meeting people from other countries, or Alison Spalding, that they have any sort of indication of problems arising before the directives came into force?

(*Dr Cottam*) My Lord Chairman, I think that it is still too early to say that there are difficulties in other countries.

Lord Walton of Detchant

13. If I may follow on from that, my Lord Chairman, is it clear that all microbiologists and, indeed, biologists in the United Kingdom who are likely to be involved in work in this field are fully aware of the regulations and is there any evidence to suggest that any unauthorised work or experimentation has been done? That is the first point. Secondly, I should like to ask you whether you have a formal relationship with the Department of Health's newly established committee on gene therapy? Where does the responsibility for work in that field fall? Does it fall to you or does it fall to them or to both, and where is the borderline?

(*Mr Brown*) If I may, my Lord Chairman, I will ask Andrew Cottam to deal with the first point.

(*Dr Cottam*) There has been a high standard of compliance in the United Kingdom with the regulations in this area to date. There have clearly been cases where people have not been in full compliance with the regulations and where that has been the case we have taken action quickly to ensure that they do.

(*Dr Spalding*) On the question of gene therapy, my Lord Chairman, it is true to say that both the Department of Health and the Health and Safety Executive, and in some cases the Department of the Environment under their release regulations, would have an interest in this area. The Department of Health obviously would lead on any aspect to do with patient treatment and health. We as the Health and Safety Executive would lead on implementing contained use regulations as they might apply to gene therapy and worker safety related to nurses who are administering the therapy. If there was a possibility that there could be any release from the gene therapy, and it is not always clear that there will be, then that might in fact come under the deliberate release regulations although we do not know of any cases yet that that would in fact happen. As far as the committee goes there is not in fact at this present time a formal connection. It is a very new committee although we are certainly talking to the secretariat of that committee.

Lord Gregson

14. If I may just follow up here, my Lord Chairman, you have a statutory duty to protect the public. It is not often implemented because there are other conflicting duties with other bodies within government. You have an overriding statutory duty. On the question of release, where do you stand?

(*Dr Buley*) My Lord Chairman, the general area of product safety is nearly always governed by the more specific regulations, and where it is governed by the more specific regulations then we do not seek to move in there. As you will know, my Lord Chairman, section 3 of the Health and Safety at Work Act theoretically could cover everything and where there are more specific regulations clearly they take precedence. In this case the deliberate release regulations, which are concerned specifically with product safety, would be the ones that matter.

15. So you suppress your statutory duty and let somebody else lead, in effect?

(*Mr Brown*) My Lord Chairman, I think that it is just worth making the point that we have instantly or very soon will have a memorandum of understanding with the Department of the Environment so that the role that we need to play, as it were, in the border territory between us is clearly specified and we each understand our respective roles.

16. But in fact you have not got the memorandum of understanding, as I understand it?

(*Mr Brown*) Yes, we have.

17. You have got it?

(*Mr Brown*) Yes.

18. Is it a public document?

(*Mr Brown*) No, it is not at this minute, but we have it.

19. May I ask then, my Lord Chairman, whether we could have a copy of it?

(*Mr Brown*) Yes, my Lord Chairman.

Baroness Platt of Writtle

20. On the question of statutory duties do operators have a statutory duty to give you all relevant information, including perhaps near accidents?

(*Mr Brown*) Yes.

Lord Walton of Detchant

21. My Lord Chairman, I have two more questions that I should like to ask, if I may. In relation to the classification of organisms for contained use in groups I and II is the classification regularly reviewed? Is there any evidence to suggest, for

[Lord Walton of Detchant *contd.*]

example, that through mutation it may be necessary to shift an organism from one group to another? The second question is this. In relation to the individuals and groups or departments involved in type A activity, which is plainly research and development, much of that will be done in universities and perhaps in independent research organisations, but some surely will be done in the research division of commercial organisations. Now if that is going on what is the mechanism whereby they can move from type A to type B activity? Do they have to come to you with a formal proposal to seek permission to move into commercial exploitation?

(*Mr Brown*) I will ask Dr Spalding to deal with the first of those questions and Dr Smith to deal with the second, my Lord Chairman, if I may.

(*Dr Spalding*) On the question of whether something like mutation could in fact mean that a gene was placed from group I to group II, it is true to say that if a mutation did in fact occur and it affected the criteria that you have to consider in schedule 2 to the regulations, thereby creating in some way a group II organism from a group I organism, then it would become a group II organism and would be subject to notification of group II organisms. But just a general mutation might not in fact affect any of the properties that you have to look at.

(*Dr Smith*) On the point about type A activity, my Lord Chairman, as you rightly say some activities within industrial organisations could be type A if they were at the research stage. There is no question of needing permission to move to type B. One just does move willy nilly into type B if one stops doing research and starts manufacturing a product, and then the person doing that would be subject to slightly different duties. The only really significant effect would be if the activity moved from being one that did not call for consent to one that did call for consent, in which case the notifier would have to come back to the executive and seek that consent.

Chairman

22. Have there been a number of incidents where you have been obliged to enforce the regulations and, if there have, what do you do?

(*Dr Cottam*) To date, my Lord Chairman, we have not enforced the 1992 regulations.

23. Is that because they are too recent?

(*Dr Cottam*) They are too recent, yes. But certainly under the previous legislation we have issued enforcement notices to ensure compliance with the legislation.

24. Are these numerous?

(*Dr Cottam*) There have been 14 in total under the 1989 regulations.

Lord Flowers

25. My Lord Chairman, may I ask what is a fairly basic question for us right at the beginning of this enquiry. I have this guidance on regulations, which I presume comes from you?

(*Mr Brown*) Yes.

26. It is the sort of thing that one expects to see: inevitably it is of a very bureaucratic and administrative nature—like "Regulation No 17 this does not apply in Northern Ireland", that sort of stuff—but what I do notice is the total absence of any quantitative or scientific information in it, as far as I can see. It seems to me entirely of an administrative nature. Somewhere or other you must have criteria for how hazardous is something, what quantity, how much can be released, in what circumstances and stuff like that, and it is that which I think we need to know at this stage rather than what is in this guidance, which we need to know at a later stage.

(*Mr Brown*) Yes, you are making the general point that we should accept that that gives you the firm rules of the game but the detailed guidance about the things that every-day people are concerned about needs to be added to that and, indeed, we should expect to be moving very much more to that.

27. Is there something you can give us that gives us some idea?

(*Dr Spalding*) Perhaps I may come in on that, my Lord Chairman. This is, of course, guidance to the regulations so it is necessarily, as you say, legalistic. In fact, ACGM, the Advisory Committee for Genetic Modification, does in fact help to produce detailed guidance, that is, practical guidance, for researchers. At the present time it has 11 guidance notes. They will have to be updated to comply with the new regulations, but there is already a great body of information in those that researchers regularly use on a day to day basis.

28. I am sure that there is, but we do not have it.

(*Dr Buley*) We can certainly supply copies if you would like, my Lord Chairman.

29. Yes, please.

(*Mr Brown*) Dr Cottam could perhaps say a word or two about the impact as inspector.

(*Dr Cottam*) In addition to that, my Lord Chairman, we seek to provide advice to people involved in this technology when we are carrying out site visits in addition to the written information that is provided.

Lord Soulsby of Swaffham Prior

30. My Lord Chairman, I want to go back to the question of adverse reactions or effects that are reported to you. How closely do you monitor these not only in this country but in other countries and what do you do if adverse effects are reported, say, in the United States of America or in Europe?

(*Dr Smith*) I was not quite sure whether the noble Lord was referring to adverse effects on human health or the environment, my Lord Chairman, or on competiveness?

31. On the environment but, since you are concerned with monitoring these products, shall we say in human health and the environment. You have a reporting system. How wide is this? Is it only national or is it world wide that you take note of these adverse effects and, if so, what is the action that you would take if a report was coming to you, say, from the United States of America of an adverse effect? Would you alert the people here on this? What would happen?

[Lord Soulsby of Swaffham Prior *contd.*]

(*Mr Brown*) My Lord Chairman, the OECD has very well established machinery for bringing together the views and experiences of the member countries of OECD which for practical purposes include almost all those countries that are significant in this field of our technology, and in general that would be the means by which we should get in information about adverse effects if they occurred. The United Kingdom itself or the Health and Safety Executive itself does not have a specific responsibility to monitor the rest of the world, but we do use the OECD mechanism and should get a good deal of intelligence through that.

32. It would be unrealistic to ignore the rest of the world?

(*Dr Buley*) Yes, I think that it is true to say also that we certainly keep abreast of all the research and we should certainly involve the Advisory Committee on Genetic Modification if a particular piece of research indicated that there was a problem that needed to be considered and then undoubtedly the Advisory Committee on Genetic Modification would take that into consideration in updating, changing or introducing some new guidance, so we certainly do keep abreast of this whole area nationally, and internationally through the OECD.

Lord Gregson

33. Is there any mechanism within the Community for monitoring this?

(*Dr Buley*) Yes, as with all directives, there is a technical progress committee and a so-called competent authorities committee set up that will meet regularly and review the workings of the directive and the clearance procedures so that there is a mechanism there, that is, a standing committee mechanism.

(*Dr Smith*) The directives themselves do also contain requirements for the exchange of information between Member States via the EC Commission about accidents that have been reported in any one of them.

Baroness Platt of Writtle

34. My Lord Chairman, perhaps I may ask two questions here. One is related to the inspectors that you mentioned a few minutes ago. In paragraph 17 of the submission I notice that they normally have a degree and they normally undergo a year's training programme before joining the team. I was rather surprised that it was not required that they have any industrial or commercial experience, whatever you like to call it?

(*Dr Cottam*) My Lord Chairman, that is referring to the training that they receive once they arrive in the Health and Safety Executive, but we specifically recruit people who have a background and experience in the technology so that all of the staff currently working in this area in my part of the organisation do have that experience.

35. Thank you. Then secondly a very short question: when was the Royal Commission 13th report?

(*Dr Buley*) Three years ago, I think, July, 1989.

Chairman

36. We have heard a bit while we have been beginning our investigation about horizontal and vertical regulations. I think we know vaguely what they mean. From a technical point of view—and by that I mean scientific technical rather than administrative technical—is there anything to choose between them? Is one better in the sense of offering more protection than the other?

(*Dr Smith*) I think, my Lord Chairman, that the answer to that is that from a strictly scientific and technical point of view there is no difference at all, you can do it either way. Either regime, provided that you make sure that the regulatory body receives the right information and can take the appropriate action will serve the purpose. There is a drawback so far as work place health and safety is concerned to a vertical based system if only because there are almost bound to be gaps in it. Work place health and safety does not really break down conveniently into product categories. In so far as one may be doing very early stage research work it is probably not possible to say what products it is associated with at all, so there is a perhaps not a technical and scientific but a very practical advantage to horizontal regulation in the work place. The question of product safety and product release is a broader one that you may want to go on to.

Lord Gregson

37. You cannot really apply horizontal regulation to a product as a product, can you?

(*Dr Smith*) You could. Again, you could do it either way.

38. It would stretch your mind a bit, would it not?

(*Dr Smith*) You could set up a regulatory regime under which products as a whole were scrutinised for risks that might be associated with them by virtue of their biotechnological origins. You could do that, or you could break it down by product category. The position that we have taken, I think, is that where products are to be vertically regulated anyway because of the sorts of products that they are, then it makes entire sense—there is no argument about this in any quarter, I do not think—to have any biotechnological scrutiny incorporated in that procedure. The question becomes a little bit more open if we consider classes of product or individual products for which there is no particular reason to have a vertical regulatory system other than the biotechnological one.

Lord Perry of Walton

39. The categorisation of GMOs for contained use of the two groups I and II is based on pathogenicity. Is there any other categorisation because GMOs include bacteria, viruses, parasites in mammals—it can be anything. Are the same regulations applicable or are they categorised to cover the differences?

(*Dr Spalding*) The group I, group II, categorisation is not strictly based on pathgenicity. It is obviously a major part because if something is a pathogen that is a serious concern and a serious hazard. It is also based on various other factors, for instance, the actual modification that has taken place is looked at.

[Lord Perry of Walton *contd.*]

You have to decide whether the DNA that has been inserted or the vector, the way it has been inserted, can cause any problem—whether it maybe can pass on the DNA to organism other is one example—so it is not just based on pathogenicity, although of course that is a major point.

(*Dr Buley*) There is a separate categorisation for non micro organisms. The groups I and II refer only to micro organisms.

40. But it would cover parasites, cellular organisms, viruses?

(*Dr Buley*) Yes, it would.

41. Does this not lead to over-elaboration of the regulations because of the variability of the thing that you are regulating?

(*Dr Smith*) In fact, my Lord Chairman, it leads to greater simplification. It is a fairly broad and in a way rough and ready categorisation. It would be possible to have a much more refined classificaiton system taking into account the different types of organisms there are which you have mentioned and perhaps also resolving more finely the different kinds of effects they have, but there is something of a trade off between that sort of specificity and complexity and elaboration in the regulations. What we have gone for, based on the directives of course, is a simpler system which divides organisms into those two principal bands, the worrying ones and the not so worrying ones, and the difficulties that have arisen have been not so much in point of specificity as on precision at the margin.

Lord Renwick

42. My Lord Chairman, we have nearly got to a concrete example there. We have been talking very theoretically and very much in general and I wondered whether Dr Cottam could perhaps give some examples, for instance, of one of the 14 instances in which he had to apply the regulations and perhaps some areas in which they are watching for problems in the future?

(*Dr Cottam*) My Lord Chairman, the examples of enforcement action that I referred to were under the 1989 regulations so it was under the previous system of legislation. In those cases action was taken for a number of reasons, which included failure to notify under the 1989 regulations that GM work was being carried work and failure to carry out risk assessment and to provide suitable facilities for the work. Those were the general areas where we took action. As far as the new legislative system is concerned what we will be looking to ensure is that suitable management systems are put in place by the people who are carrying out this work to ensure safety and that the facilities that they are providing for the work, whether that be a laboratory or an industrial production plant, meet the standards that are laid down by the guidance produced by ACGM.

Chairman

43. Are these new regulations stiffer than the old ones and, if so, why?

(*Mr Brown*) My Lord Chairman, we make it clear in our evidence that the requirements for notification of the less risky operations and the category I products are more rigorous than the previous existing ones.

44. Where does the demand for this increased rigour come from? Does it come from you or does it come from abroad or where?

(*Mr Brown*) The demand in part is a reflection of the fact that the 1989 regulations did not touch explicitly the environmental effects so that is an additional risk area. We say in our evidence that although there is very little to suggest that the risks to human health from GMOs is of any great importance or significance the same cannot be said with quite the same confidence with regard to the effects on the environment; so the fact that the new contained use regulations bring in a concern about environmental effects is an additional responsibility that the regulatory system, as it were, has to take account of. However, to put it more bluntly, my Lord Chairman, we should have been reasonably content as the Health and Safety Executive, and so far as the protection of human health is concerned, to have continued along with the 1989 basis, but frankly there was a very great deal of quite emotional argument, quite a lot of attempts by some other countries, to go even further towards rigorous regulation in the discussion of the directives and we came out with a conclusion that was the best that could be secured meeting what most Member States were prepared to accept.

45. By Member States, you mean in the Community?

(*Mr Brown*) In the Community, yes, my Lord Chairman.

Lord Flowers

46. If the containment regulations are appropriate the environment is automatically taken care of, is it not? What is the purpose of the containment regulations otherwise?

(*Mr Brown*) Because the containment may not be in every situation secure. You can have a contained operation in which the containment breaks down, and in some low-risk activities there may be routine discharges.

Chairman

47. If we may go back to the question that I raised earlier about horizontal and vertical, I understand that the United States regulations are moving from horizontal to vertical—that is the general idea, I know. Are the British regulations likely to follow?

(*Dr Smith*) My Lord Chairman, I think it is probably necessary to tease out the American situation a little more fully before going beyond that. It is perhaps not quite true to say they are moving in the United States from horizontal to vertical. So far as product release is concerned, which is the area that we are mainly talking about here, it always was vertical and it is just really that some changes have been taking place within what I think we indicate is a fairly complex vertical system. There have been some adjustments in the regulatory regime as it is now, in some cases towards greater relaxation, in some cases towards tightening and in some cases towards a more explicit recognition of biotechnological factors. At

[Chairman *contd.*]

the same time there has been some scrutiny at federal level of the whole system, particularly at the discretion that the agencies have in America to give different levels of oversight to GMO activities within the legislative structure that they have. That scrutiny led to a policy white paper last year by the Office of Science and Technology Policy, which recommended a risk based approach and did argue pretty unexceptionably that it is the properties of the product and the risks assocaited with the product that matter, not the fact that it is a biotechnological product per se. What all that means really is that for the time being the American system, which has been largely vertical as far as products are concerned, has not really changed all that much and the United Kingdom system does not really need to be adjusted to fit. As we said earlier, my Lord Chairman, we already do have provision for incorporating the and intention to incorporate, product clearance procedures into vertical legislation where it is going to exist anyway. As the Department of the Environment will explain soon, the United Kingdom system based on risk assessment with the possibility of simplifying procedures once it is established that products warrant simpler procedures is not really so very far form the United States system.

48. Already?

(*Dr Smith*) Already, my Lord Chairman, yes.

Lord Gregson

49. There are signs, of course, that the United States system is beginning to recognise the need for product liability insurance. It is the insurance industry in effect which is driving the method of regulation because if you do not get insurance you do not get a product, period. Since insurance is an international operation surely it is going to dominate the whole field eventually?

(*Mr Brown*) In a number of fields American practices are driven by insurance and we have not yet in general had the same impact as one might have predicted. I think that it does depend a very great deal on the specific culture in which the law is applied.

(*Dr Buley*) My Lord Chairman, it is perhaps just worth adding here as regards the future that there is specific provision in the European directive that if a product is regulated by another directive, so long as that directive makes provision for risk assessment if genetic modification is involved then it can be exempt from this directive, and as far as we know there is a large number of such directives coming on to the stocks. I think therefore that the simple answer to your first question is, yes, in Europe, as these other directives come on to the stocks and they regulate medicinal products, veterinary products and all the rest of it vertically, so long as they have some provision in there to take account of the genetic modification side as laid down, they will be exempted from this horizontal regime.

Lord Walton of Detchant

50. My Lord Chairman, perhaps I may ask one short question relating to human health following on from what Lord Soulsby said about adverse effects. There was a suggestion that so-called genetically engineered insulin was having more side effects and producing more hypoglycaemia attacks than the traditional porcine or bovine preparations. Now presumably that would have been reported to the committee on the Safety of Drugs in the first instance, and the fears turned out to be unfounded. However, if it had proved to be a substantial case would it then have been your responsibility to examine the process? Would it have been referred to you by the Committee on the Safety of Drugs, for example?

(*Mr Brown*) I do not think that it would.

(*Dr Spalding*) As a drug it would come under the appropriate legislation and appropriate departments to deal with a medicine.

Chairman

51. Time is getting on now, I am sorry to say, but I have just one final question before we finish. I understand that EC directives 219/90 and 220/90 are being reviewed in their importance for us. When is full implementation expected?

(*Mr Brown*) My Lord Chairman, full implementation should by now have been achieved in the sense that all Member States ought to have had appropriate legislative provision to implement them. That is not yet the case. If by full implementation is meant systems that are effective and thoroughly tested and bedded down, that obviously adds a bit in a number of countries to the time scale that we are thinking of. I think that it is realistic to anticipate that any full scale review of these directives must allow some reasonable amount of time of operation, not simply of implementation of the regulations.

52. So you do not expect a review very soon?

(*Mr Brown*) I do not myself think that it will happen tomorrow, my Lord Chairman.

53. Or the week after tomorrow?

(*Mr Brown*) Or the week after tomorrow. It is fair to add that it is possible to amend and develop one or two of the annexes to the regulations by what is called technical amendment, which would not require going through the whole council amending procedure, and no doubt that will go on as necessary as we gain experience, but I do not myself see a major review of these directives until we have a decent amount of working experience.

Chairman] That is very precise, Mr Brown, thank you. I think that we will have to draw this to a close there. We obviously have not covered the ground totally. If there are any further points in amplification that you wish to let us have, please write to us and let us know. It is just possible that we may write to you later on. Thank you very much.

Written evidence from the Department of the Environment

1. *What is your interest in biotechnology?*

1. The Department's main interest in biotechnology centres around measures to reduce the risks associated with the release of Genetically Modified Organisms (GMOs) into the environment. Last year the Department cleared 15 releases of GMOs. However, the Department's interest in whether GMOs might cause environmental "harm" also extends as far as the contained use of GMOs, but in this case the capacity of the GMOs to cause harm is contingent on the escape from containment and on their coming into contact with the environment.

2. The Department is also interested in promoting applications of biotechnology which confer environmental benefits. The Environmental Technology Innovation Scheme (ETIS), which DoE fund jointly with DTI, is sponsoring a number of projects involving biotechnology (but not GMOs) which aim to solve environmental problems in an innovative way.

3. Other than DoE, several other Departments also have an interest in the control and regulation of GMOs. HSE has operated a regulatory scheme controlling GMOs for some years and lead on contained uses. MAFF have an interest in deliberate release where this impinges on agriculture, food and fisheries issues, while DoE, SO and WO are respectively responsible for the environment in England, Scotland and in Wales. Northern Ireland operates a separate, but parallel, system.

4. In 1989 the Royal Commission on Environmental Pollution (RCEP) published their thirteenth report, "the release of Genetically Engineered Organisms into the Environment" and called for specific regulation of GMOs. This was provided for in Part VI of the Environmental Protection Act (1990), the purpose of which is to prevent or minimise damage to the environment from GMOs. The Act provides the first specifically environmental controls over GMOs. Previous legislation only covered human health and safety.

5. Co-incidentally, the European Commission also proposed harmonised EC regulation of GMOs, resulting in the adoption of two Council Directives in April 1990. The first of these, 90/219/EEC, deals with contained use (of microorganisms) and the second, 90/220/EEC, deals with deliberate release.

6. Directive 90/220 provides the basis for regulation of deliberate release and marketing of GMOs and ensures that a co-ordinated system of clearing R&D and products exists within the single market. Information exchange between Member States is required before consent for release can be given. In the United Kingdom, Part VI of the EP Act 1990 and the Genetically Modified Organisms (deliberate Release) Regulations 1992, give effect to this legislation and require the Secretary of State's consent for all such activities. A synopsis of the relevant legislation is attached as an annex.

7. Contained uses of GMOs are similarly regulated and these regulations, in turn, lay down common environmental and human health and safety measures for such operations. The Regulations introduce a graduated system of risk assessment, notification and consent, according to risk, for operations with GMOs in contained use.

8. The regulatory controls on GMOs are operated jointly by DoE and HSE with MAFF, SO and WO as appropriate. The split in regulatory responsibilities between contained use where, by definition, organisms' contact with the environment is prevented or minimised, and deliberate release, where contact is not so minimised, means that the Department's main activity in this field is the scrutiny of applications for consent to release GMOs. DoE is the lead department operating the system dealing with deliberate release, in collaboration with HSE, MAFF, SO and WO.

9. The system for the contained use of GMOs is operated by HSE (with DoE scrutinising environmental risk assessment). Smooth operation of the controls is ensured through a memorandum of understanding.

10. The Royal Commission (thirteenth report) advised the setting up of an advisory committee to scrutinise releases to the environment on a case-by-case basis. This was provided for in the EP Act 1990, and the Advisory Committee on Releases to the Environment (ACRE) is now a statutory advisory committee to the Secretary of State. The secretariat to ACRE is provided by DoE and there is wide representation of all interested parties either as members of the committee, or as assessors to it. Harmonisation arrangements will be made so that ACRE can advise on releases in Northern Ireland as well as in Great Britain.

11. In the second anniversary report to the White Paper "This Common Inheritance", the Government committed itself to easing the regulatory burden for low or no risk releases (including those intended for environmentally beneficial purposes). This will be achieved by streamlined administrative procedures in the United Kingdom and in Europe. The United Kingdom system for streamlining is currently one of the most advanced amongst the EC Member States.

12. The Department runs a programme of research (currently £1m per annum), in consultation with the statutory Advisory Committee on Releases to the Environment (ACRE), which aims to help the Secretary of

State ensure that regulatory hurdles are set at levels appropriate to risk. Identifying "low-risk" releases is a major priority of the programme.

13. As well as regulating GMOs, the Department also has responsibilities in regulating the use of some other products of biotechnology, which are not genetically modified organisms.

14. These are:

(i) microbial pesticides (Control of Pesticides Regulations 1986 and Food and Environmental Protection Act 1985) for which MAFF lead;

(ii) other biopesticides, for example, insect-parasitic nematodes (Wildlife and Countryside Act 1981 if organisms non-indigenous to the United Kingdom);

(iii) control of industrial discharge to land air and water (Parts I and II of EP Act 1990) and control of all discharges to waters (Water Resources Act 1991; Water Industry Act 1991).

15. The Department also has an interest in positively encouraging some aspects of biotechnology. ETIS funds activities which aim to solve environmental problems in an innovative way. Some examples of such work include the use of biotechnology for; treatment of organic contaminants in soil (bioremediation holds great promise for environmental clean-up) and treatment of coloured organics in effluent using bioadsorption.

16. Biotechnology provides a variety of analytical tools which are either of current or potential value to the Department, such as the development of rapid methods for detection of contaminants in water. Molecular diagnostic tools may also play a part in future emergency planning, in facilitating detailed study of the UK's biodiversity and in enforcing the GMO Regulations.

2. *How and why is biotechnology important to UK industry?*

3. *What future prospects and opportunities does the technology offer?*

17. Biotechnology is an enabling technology which already cuts across the functionalist notion of industry. In many cases, though not all, biotechnology is used to improve existing approaches to old applications. For example; improved plant varieties and new methods of enzyme production. In other cases, biotechnology has allowed new departures: gene therapy, novel protein production for food, and novel diagnostics.

18. Promise is shown by applications of "environmental biotechnology" such as on-site bioreactors for waste treatment, and in particular treatment of toxic wastes. The use of such green technologies may reduce costs for industry in treating wastes and may have beneficial knock-on effects on public perception and consumer confidence as well as helping to move towards a cleaner environment.

19. The growth of GMO technology in recent years has broadened the scope and shortened the timescales for "improving" organisms for specific purposes. Some applications have proved easier than others but, as technical bottlenecks are broken, the number and diversity of applications can be expected to increase. In the context of environmental improvement, possibilities exist for displacement or reduction of chemical usage in the environment and for the targeted clean-up of sites suffering from long term pollution problems. Analytical tools can also be expected to be developed to improve detection of water and land contaminants.

4. *Which developments in biotechnology raise issues of safety and how should they be addressed?*

20. The introduction of a new or novel species to a familiar environment, or the introduction of a familiar organism to a new or novel environment, presents hazards which need careful consideration. In line with the Government's policy of taking a precautionary approach to environmental protection, the solution is to carry out risk assessments on a case-by-case basis and to move forward as experience accumulates. This is the in line with the approach recommended by the Royal Commission in their thirteenth report.

21. GMOs released into the environment raise environmental and human health and safety questions because they are generated by rapid and novel techniques which produce heritable genetic changes. Genes from across species barriers and beyond can now be inserted into a wide variety of organisms for a number of specific purposes, some of which (eg biopesticides) may be intentionally harmful to target organisms. In some cases, the inserted genes or their products may persist in the environment or spread to other organisms, including humans, in ways which have potential effects which may not be obvious (for example, extending the host range of biopesticides to other, beneficial organisms). This difficulty in identifying hazards posed by GMOs was recognised by the Royal Commission's fourteenth report, "GENHAZ: A System for The Critical Appraisal of Proposals to Release Genetically Modified Organisms into the Environment".

22. The extent of the risks from GMOs is likely to vary considerably from case to case. A large degree of experience of the risks presented by the use of certain GMOs in well-defined situations, particularly in containment, has already been gathered over the past 20 years. As a result, all but a few of such operations use low risk organisms. Experience of other uses of GMOs, particularly their deliberate release to the environment, is less extensive but is growing. Scrutiny of releases at appropriate stages—for example, the

transition form small to large scale trials—allows the development of safe GMO products to be informed by the benefit of experience.

23. Some hazards identified in the risk assessment of GMOs may also exist for non-GMOs used in biotechnology. For example, the application of large quantities of naturally occurring live organisms to the environment with specific functions (for example, bioremediation; biopesticides) may present identifiable hazards, for example associated with the accumulation of breakdown products.

5. *Should biotechnology be regulated by an industry specific regime?*

24. As an enabling technology, developments in biotechnology often cross industry "boundaries". Consequently, new developments and approaches may not be industry specific. This is particularly the case with the modern molecular techniques applied to GMOs. Experimental work may be carried out in "model" systems before the technology is transferred to end use applications: such work cannot be assigned to a specific industrial sector. By its very nature, experimental work involves the unfamiliar and is consequently often of a less well defined risk than more developed work. The Deliberate Release Regulations, as well as the Contained Use Regulations, recognise this and provide for safety regulation and information exchange with our European partners on all R&D work carried out in the Community.

25. The Deliberate Release Directive also provides for regulation of products comprising, or containing, GMOs to be placed on the market and allow for a "one key, one door" approach. To achieve this, the UK has consistently pressed in Europe for the adoption of new, or the amendment of existing, specific product directives ("vertical legislation") that require a similar environmental risk assessment to that of the Deliberate Release Directive. Dual notification would be avoided by removing "vertically" regulated products from the requirements of the Deliberate Release Directive which otherwise apply to all products ("horizontal legislation"). However, new or amended "vertical" legislation is only practical when biotechnology is used widely for product development in a well-defined sector.

26. A move from "horizontal" to "vertical" regulation is likely to have little effect of the regulatory "burden" on industry. "Vertical" regulation will still require a risk assessment to be carried out and taken into account for all GMOs, in the same way as the Deliberate Release Regulations. The most likely effect of a move to "vertical" regulation is that industry might find a product approach more convenient to operate under, even though different requirements within the same "vertical regulation" would continue to apply to GMOs and non-GMOs.

27. The argument that "vertical" regulation is better than "horizontal" regulation is often misrepresented as an argument in favour of deregulation. The dichotomy is false since both approaches have as their objective the achievement of a safe technology whose benefits can be commercially exploited. "Horizontal" regulation may be more appropriate for sunrise technologies since their products will take time to become well-characterised. The move to "vertical" legislation is appropriate when industries based on the new technology become established. Government regulatory policy, as expounded in the White Paper, endorses this view.

28. R&D work will continue to be regulated across industry boundaries under the Deliberate Release Regulations. This "horizontal" regulation allows for the promotion of the sunrise aspects of the technology. The precautionary approach is designed to avoid possible set-backs should accidents occur. The single post-box for all applicants proposing to release GMOs, no matter for which purpose makes the regulatory system more transparent to the applicant and avoids the necessity to make applications to several agencies for one piece of work, as is seen in the USA.

6. *From a technical point of view, is horizonal regulation (where a product is judged through the process by which it is derived) better than vertical regulation (where a product is judged by its characteristics)?*

29. Although the Deliberate Release Directive (and the Deliberate Release Regulations) brings GMOs into the regulatory system by virtue of the process by which they are made, the assessment of risk is performed on a "product" basis. The key elements considered in the assessment are the nature of the GMO, the inserted genes it carries, the receiving environment and the nature and scale of the proposed release.

30. From a technical point of view, the information requirements currently set out by the GMO "horizontal" regulations could be as easily satisfied by "vertical" regulation, though this is not yet in place. The purpose of such information is adequately to inform a risk assessment of the organism used for the purpose proposed. The level of information required to be given must be sufficient, but no more, to inform such a risk assessment. Consequently, the specific information required, and the level of detail of this, will vary from case to case. The applicant for a consent to release has to make a decision on the relevance of specific aspects of information and on whether to provide such information in his proposal. From the point of view

of providing information and carrying out a risk assessment, there is little if any difference between compliance with "horizontal" rather than "vertical" regulation.

7. *Should regulation evolve from a horizontal to a vertical approach in each industrial or environmental application?*

31. Such evolution is already taking place. It is envisaged that the regulation of many product applications of biotechnology will evolve towards a "vertical" approach in those sectors where the technology is used extensively, provided an adequate risk assessment is carried out.

32. Council Directive 91/414/EEC on Plant Protection Products provides for a risk assessment of the environmental impact of plant protection products corresponding to that in the Deliberate Release Directive. Although a decision on a Commission proposal on the environmental risk assessment has not yet been taken by the Community. The UK has supported the principle of "disapplying" plant protection products from the market provisions of the Deliberate Release Directive. Other proposals for "vertical" legislation are at various stages of negotiation within Europe. The EC Medicinal and Veterinary Products Regulation as well as regulations dealing with of novel foods and of animal feedingstuffs provide for such GMO integrated "vertical" regulation and are at various stages of implementation or negotiation.

33. The Royal Commission recommended (in their thirteenth report) "horizontal" regulation and strict case-by-case review of proposed releases of GMOs. There is a clear need for "horizontal" regulation of GMOs used in R&D to continue, as this approach is considered best to provide simple, transparent safety regulation of a growing technology. It also ensures that GMOs in products not covered by specific product legislation will be appropriately assessed for risk to the environment.

8. *How do current regulations compare with those of other competitor countries*

— in Europe

— in the Far East

— the USA?

34. The Deliberate Release Regulations implement Council Directives 90/220/EEC, which has an Article 100A treaty base. The Directive is designed to provide a "level playing field" across Europe. Not all Member States have yet implemented, although considerable progress has been made. At present, six Member States have notified legislation to the Commission; France, Germany, Ireland, Denmark, the Netherlands and the UK. Around 100 R&D releases have taken place in Europe since October 1991 (the target date for implementation of Directive 90/220).

35. Some other countries outside the EC have either brought in largely similar regulations, or are in the process of doing so. Hungary already has a system in place which is nearly identical to the EC system and Austria, Norway, Sweden and Switzerland are all in the process of developing compatible systems to come into line with the provisions under Article 100A as part of the move towards harmonisation in the European Economics Area. A recent mandate to the European Standards Organisation (CEN), issued under Council Directive 83/119/EEC on Technical Harmonisation and Standards, aims to develop standard methodologies in order to satisfy some of the information requirements in the Deliberate Release Directive. The active participation of EFTA countries in this initiative inspires confidence in wider harmonisation.

36. In the Far East, Japan is the chief competitor in biotechnology. Japan participates in OECD work which identifies common approaches to regulation of biotechnology. Japan relies entirely on guidelines rather than biotechnology-specific regulation. Their guidelines for contained work follow closely US National Institute of Health (NIH) guidelines and are process based ("horizontal"). Japan's guidelines on releases follow closely guidance from OECD, which advocates a step-by-step approach and which was also the progenitor of the EC GMO Directives. However, very few releases have taken place in Japan which has effectively run a *de facto* moratorium until recently. Consequently, the Japanese have less experience of these operations than either Europe or the US. Japan has no regulations at present, but closely follows the above-mentioned guidelines.

37. Other states in the Far East hold widely diverging views. Several of the ASEAN states were vocal during the negotiations leading to the Convention on Biodiversity and in the Agenda 21 discussions within UNCED. There appears to be general backing amongst ASEAN states for a mechanism of prior informed consent before the import of GMOs and for an eventual international agreement on biotechnology safety. China has reportedly carried out a large number of field releases of GMOs, including at least one at full commercial scale. There does not appear to be any regulatory constraint on such work in China although all releases are subject at least to indirect state control *via* the respective research agencies and the Chinese consult widely with international experts prior to carrying out releases.

38. In the USA, the regulatory picture is complex and is in a state of flux. At present, regulation of products is carried out using a "vertical" approach at the Federal level. Regulation of biotechnology is thus split across sectors and across government agencies. The US Department of Agriculture (USDA) is responsible for issuing permits under the plant health act for the release of genetically modified crop plants only when these

are constructed using a "plant pathogen" (*Agrobacterium* vectors). More direct means of introducing DNA (for example, "biolistic" methodologies) fall outside the scope of these regulations.The US Environmental Protection Agency (EPA) plan to bring in a second set of regulations (under the Federal Insecticide, Fungicide and Rodenticide Act—FIFRA) to cover the release of "plants with pesticidal properties" (plants genetically modified to express pesticidal products). Further, a permit is required from the US Animal and Plant Health Inspection Service (APHIS) to move such plants from one state to another. If the product is intended to be used as a food, then approval must also be obtained from the Food and Drugs Administration (FDA).

39. If genetically modified microorganisms are to be released, the appropriate regulatory body is the EPA, who are in the process of bringing in separate controls under FIFRA and under the Toxic Substances Control Act (TSCA).

40. Some states (Minnesota and North Carolina) are developing their own legislation, since they see the Federal system as leaving gaps. In August 1992, a new chapter (Chapter 4420) of the Minnesota State Statutes came into effect This, together with modifications to Chapter 4410, provides for control of the release of "Genetically Engineered Organisms" (a "horizontal" approach). The scheme includes requirements for the preparation of an "Environmental Impact Statement", review by a Genetic Engineering Advisory Committee, publication of a public notice by the applicant and full administrative cost recovery. Exemptions from the scheme are possible, *ad referendum,* if a compatible Federal permit is held, nevertheless, in some cases a number of separate permits may be required from different agencies for the same release (eg USDA for use of plant pathogen, APHIS for transport across state lines, FDA for novel food, consultation with EPA for plant with pesticidal properties).

41. At the experimental level in laboratories, NIH guidelines (which are "horizontal") require regulatory scrutiny of work involving GMOs and broadly similar procedures operate there as are described under the United Kingdom's Contained Use Regulations.

42. Finally, APHIS have published proposals for a system of negative consents (24 hour advance notification) for a limited number of specific crop/trait combinations. This development is being paralleled in Europe by the development of "simplified prodecures" under Directive 90/220. Both systems propose similar criteria.

9. *What are the consequences, or likely consequences, of the regulatory regime on competitiveness of the United Kingdom industry, in particular as regards*

(1) research

(2) product development

(3) investment

(4) location

(5) sales and marketing

43. All of the major actors in the biotechnology field are members of the OECD, where there is a considerable amount of work carried out directed at mutual acceptance of national regulations and of data supporting risk assessment. One explicit aim of this work is to aviod the creation of non-tariff barriers to trade in products of biotechnology. Consensus buiding in OECD is thus a high priority for the United Kingdom and for other countries. Much progress has been made in developing such consensus over a number of issues: indeed, the two EC GMO directives evolved directly from OECD publications.

44. Further, the Government has expressed its commitment to seeking wide international agreement on risk assessement and risk management in the second report to the White Paper, "This Common Inheritance". This commitment follows on from the lead role the United Kingdom and the Netherlands took in pushing for agreement on biotechnology safety in Angenda 21 during UNCED.

45. Other mechanisms also have effect on the use of international environmental safety standards for biotechnology. The Biodiversity convention contains reference to a necessity for countries exporting organisms first to receive the "prior informed consent" of the importing country. All the EC Member States have signed the convention, though the US has not done so as yet.

46. International standardisation and mutual acceptance of data aim to reduce non-technical barriers to competitivity, so the effect that specific regulation of biotechnology is likely to have on the UK's competitive position will to some extent depend on the success of these efforts. It is thus a key objective that international agreement on safety standards be as similar to UK regulatory standards as possible, even if the mechanisms for achieving these are different. In order to compete successfully, UK industry will need to meet the safety standards agreed upon, particularly in OECD and the internal market.

47. The research and development stages of marketing a product will bear the brunt of compliance with standards. Compliance costs will consist of two elements, firstly the administrative costs and opportunity costs associated with applying for a consent, and secondly, and perhaps more significantly, the costs associatedwith generating data to satisfy regulatory requirements. DOE has already carried out a study of

compliance costs to industry using GMOs which, compared to the size of the "biotechnology sector", are forecast to be low. Relatively little of the UK biotechnology industry yet depends on GNOs.

48. The key to keeping compliance costs to a minimum, whilst still ensuring adequate environmental protection, is to keep the level of detail required in applications for consents to an appropriate minimum. The Regulations, like the EC directive they implement, make clear that the extent and level of detail of information required should be supplied only in so far as it is relevant to the risk assessment.

49. DOE has already, in consultation with ACRE, put into place a mechanism for "streamlining" the administrative procedures which apply to applications to release GMOs for which considerable experience has been gained. On the European front, the UK competent authority has taken the initiative in proposing simplified procedures under the Directive. Proposals have also been put forward by France and Belgium. Furthermore, the Summary Notification Information Format (SNIF) which serves as the basis for information exchange between Member States, can be modified by Article 21 committee, as can the majority of the Annexes (which spell out the detailed information requirements) to the Directive. It is likely that this will take place during the coming months. The Government has expressed in the 2nd Year Report of the White Paper on "This Common Inheritance" its commitment to encouraging development of "green" applications by fast-tracking. The measures taken both domestically and on a Community-wide basis are important stages in accomplishing this.

50. The Directive makes provision for products to be removed from its scope if they are covered by Community legislation which provides a similar environmental risk assessment. The Government's policy is to continue to press in the Community for appropriate product-based controls and then to introduce appropriate domestic legislation.

51. The primary powers in Part VI of the Environmental Protection Act 1990 have provision for "tiered" controls (from risk assessment only, through notification, to consent), with possibilities of exemption in all cases. This provides for maximum flexibility in regulatory control which can thereby take account of any possible future changes regarding the necessity for consents laid down in Directive 90/220 as Europe accumulates experience.

52. The UK thus has a system already in place for reducing compliance costs when this is justified by low risk and it is Government's policy to strive to extend this modest start to the European system. The provisions in the EP Act 1990 allow the process to be as flexible as regulatory schemes in other, non-European, countries.

53. One additional measure in the Regulations which has already been taken to minimise compliance costs is the provision for applicants for consents to include whole programmes of research (subject to limitations) in one application, as long as the environmental impacts of these can be addressed in a single risk assessment.

54. Regulatory development must not get out of step with public confidence in the technology.

10. *Is there a danger that the present regulatory regime will prevent the exploitation by British industry of research conducted in the UK science base?*

55. There is no obvious reason why this should be so. Furthermore, the numbers of applications for consents under the new regulations are at least as high as the numbers of notifications under the previous regime. In the first month of operation, since 1 February 1993, seven applications have already been received.

56. Fees and charges are levied to cover the administrative costs of processing applications for consent and the enforcement work of Inspectors, but this is in line with Treasury policy which is to have full recovery of costs. The present scheme does have tiered fees to take account of the "streamlining" of certain types of application for consents, where risks are low and well defined, and the criteria for streamlining will be adapted regularly to take account of experience gained with some GMOs . Furthermore, a single fee might cover a multi-year programme of work; this will help to reduce the cost to the user.

11. *How best can issues of public acceptance be addressed?*

57. Transparent regulation is one way to underwrite public confidence in the safe management of biotechnology. The UK Regulations provide for disclosure of information relating to an application for a consent on a public register and require the applicant to place an advertisement briefly summarising the intended work. These measures will allow people in the locality of release sites to keep themselves advised of what is going on. Further disclosure is provided for by EC Directive 90/313/EEC on the freedom of access to information on the environment. This is implemented in the UK by The Environmental Information Regulations 1992. These regulations impose an obligation to make environmental information available on request, subject to certain confidentiality restrictions.

58. All applications for consent to release GMOs are considered by the Advisory Committee on Releases to the Environment (ACRE), upon which are represented all interested parties. The scrutiny by ACRE and a strong, well-respected regulatory regime will each help to underwrite public confidence in products of this technology.

12. *What other factors do you consider will play a crucial role in the competitiveness of the UK biotechnology industry?*

59. Whilst issues of industrial competitiveness are largely for DTI, agreement on international safety standards for the use of biotechnology will do much to ensure unnecessary barriers to the competitivity of the UK biotechnology industry are avoided.

GENERAL BACKGROUND: SUMMARY OF RELEVANT LEGISLATION

1. The Genetically Modified Organisms (Contained Use) Regulations 1992, in conjunction with the Health and Safety at Work, etc Act 1974 and the European Communities Act 1972, give effect to Council Directive 90/219/EEC on the contained use of genetically modified micro-organisms, which lays down common environmental and human health and safety measures for such operations. These Regulations also cover the human health and safety aspects of contained uses of larger GMOs (eg plants and animals), which are not addressed in Directive 90/219/EEC.

2. The Contained Use Regulations 1992 introduce a graduated system of risk assessment, notification and consent, according to risk, for operations with GMOs in contained use (ie facilities where contact with the environment is prevented or minimised through appropriate containment).

3. The environmental aspects of contained uses of larger GMOs are controlled under provisions in Part VI of the Environmental Protection Act 1990 (section 108(1)(a) and (5) and The Genetically Modified Organisms (Contained Use) Regulations 1993. The requirements in relation to such organisms is to do a risk assessment and keep an appropriate record for 10 years.

4. The Genetically Modified Organisms (Deliberate Release) Regulations 1992, in conjunction with Part VI of the Environmental Protection Act 1990 and the 1972 Act, give effect to Council Directive 90/220/EEC on the deliberate release into the environment of genetically modified organisms. The Directive lays down common environmental and human health safety measures in relation to the R&D release and marketing of such organisms as or in products. The Regulations require the Secretary of State's consent for all experimental releases of GMOs or their placing on the market as or in products.

5. The Genetically Modified Organisms (Deliberate Release) Regulations 1993 correct a minor drafting defect in The Genetically Modified Organisms (Deliberate Release) Regulations 1992.

6. The provisions on disclosure of information in relation to both contained use and deliberate release are based on the two EC directives. They also take account of EC directive 90/313/EEC on the freedom of access to information on the environment. The latter is implemented in the UK by The Environmental Information Regulations 1992. These regulations impose an obligation to make environmental information available on request, subject to certain confidentiality restrictions.

7. Both GMO directives specify that, with certain exceptions, competent authorities may not divulge commercially confidential information. Information relating to the exceptions (eg the description of the GMO) cannot be kept confidential. However, such information may be framed, where appropriate, in a way which protects intellectual property rights since the Directives imply an overriding obligation on competent authorities to protect such rights.

Examination of witnesses

Dr D J Fisk, Chief Scientist and Director, Directorate of Air, Climate and Toxic Substances, Dr H Marquard, Biotechnology Unit, biotechnology regulation, and Dr I Gillespie, Biotechnology Unit, research, monitoring and standards in biotechnology, Department of the Environment, called in and examined.

Chairman

54. Welcome to the Committee. Would you introduce your colleagues to us, tell us what they do and what the background is briefly and, if there is any initial statement that you wish to make to amplify your written evidence, we will be very pleased to hear it.

(*Dr Fisk*) Thank you very much, my Lord Chairman. Dr Helen Marquard's responsibilities in the department are for the implementation of the directives 219/90 and 220/90, and Dr Iain Gillespie is responsible for the development of risk assessment standards in the Department of the Environment. As you know, my Lord Chairman, I am the Director of Air, Climate and Toxic Substances Policy in the department and the department's Chief Scientist. I have only a short introductory remark to make, my Lord Chairman, which is to say that the department welcomes the Committee's enquiry. It is a primary concern of my secretary of State that we should meet our environmental standards with the very minimum of burden and the minimum adverse effect on our competitiveness. Therefore, we shall be following your proceedings with great interest.

55. Thank you. These two parameters might not be too easy to bring together. We have heard this morning that the Health and Safety Executive played an important part in these regulations in the area

[Chairman *contd.*]

obviously of health. To what extent does your environmental responsibility overlap with theirs?

(*Dr Fisk*) I think that the easiest way that we could describe it is that my department leads on environmental aspects of biotechnology in general, particularly genetically modified organisms, and therefore we do have some peripheral responsibility for issues that are to do with biotechnology but not specifically genetically modified organisms. Our primary role, however, is in the control and regulation of deliberate releases of genetically modified organisms. That role is exercised through the Genetically Modified Organisms (Deliberate Release) Regulations, which date from last year, and they come under the Environmental Protection Act. We play a secondary role to the Health and Safety Executive in the regulation of contained use of genetically modified organisms. That role is secondary, as indeed the Health and Safety Executive have explained, since by definition genetically modified organisms in containment are intended not, as it were, to get into the environment although circumstances may arise, of course, in which that occurs.

56. We did hear that sometimes contained material gets out. When it gets out does it cease to be the responsibility of the Health and Safety Executive and does it become the responsibility of the Department of the Environment?

(*Dr Fisk*) The issue of considering the degree of containment, as I described it, would of course be for the Health and Safety Executive as the lead department. They would of course take into consideration issues that we might raise that would relate to the possible release should that containment fail, that would be the relationship. If a species were to be released it would then fall under the terms of the Environmental Protection Act in respect of what harm and damage it might do. As far as the issue of consents for contained use is concerned the Health and Safety Executive would be in the lead.

57. So you have some clear responsiblity of a kind?

(*Dr Fisk*) My Lord Chairman. The Health and Safety Executive and ourselves have gone to some effort to make sure that the seams are fairly tight between us because there is nothing more irritating, to industry than not to be clear where responsibilities lie. Indeed, some of the time that it took to produce our respective regulations was to iron out a smooth operation between the two regulatory authorities. It should be very clear to industry whom they should apply to for their consents and the internal procedures to ensure these overlapping responsibilties work smoothly.

58. Who co-ordinates this?

(*Dr Fisk*) That relates entirely to whether the issue is concerned to a release or is concerned to a contained use. As I described, there is a lead department, as it were, co-ordinating in each one of those cases.

Lord Flowers

59. My Lord Chairman, may I just chip in a second to ask whether there have been releases that have caused you concern?

(*Dr Marquard*) My Lord Chairman, there is a departmental advisory committee on releases to the environment which advises the secretaries of state and the Health and Safety Executive on all aspects of safety of releases prior to the release taking place. The releases that have taken place have all been small scale so far and there has been adequate control and considerable monitoring to ensure that there have been no adverse effects.

60. You are speaking of planned releases, are you not?

(*Dr Marquard*) Yes.

61. Have there been any unplanned releases that have caused you concern?

(*Dr Marquard*) There have been no unplanned releases to our knowledge. There are inevitably some incidental releases from contained use facilities, but that is all.

Lord Gregson

62. Is it not true that there is a problem arising from sewage treatment related to a possible source of release? There are certain hormonal releases that are now well documented. In fact, I think that Dr Fisk authorised a report on this some time ago.

(*Dr Gillespie*) My Lord Chairman, I am sorry to say that we are not aware of the specific releases that you are referring to. If you could perhaps elaborate we should do our best to answer.

63. Fish changing sex?

(*Dr Fisk*) Ah, this was relating to quite a recent report, but there is not one, I think, specifically related to genetically modified organisms, my Lord Chairman.

64. I accept that. I am illustrating that there are routes via sewage where you could get a genetically modified "something", at least. It has already happened on hormonal releases caused through medicine?

(*Dr Fisk*) Dr Marquard will explain the position on wastes as they relate to regulation.

(*Dr Marquard*) My Lord Chairman, the position is that if somebody is intending to do a contained operation they are required to do a risk assessment. That written assessment must take into account all possible routes by which the organism could enter the environment and then assess what the impact of those organisms on the environment was going to be, so that there are mechanisms there for taking that in hand.

Lord Whaddon

65. Bearing in mind the great importance of your work are you satisfied that you have adequate resources to carry out your work effectively or are there examples slipping by you that you do not have the resources to follow?

(*Dr Fisk*) My Lord Chairman, at the moment we fully meet the required statutory turn around for all applications to us. If industry meets the ambitions that it has for future expansion then clearly we should be under a much more stretched position. But at the moment we are hoping that we are providing a good service to industry and at the same time having

[Lord Whaddon *contd.*]

adequate surveillance for the protection of the environment.

Chairman

66. What are the major risks to the environment from biotechnology, on which you presumably concentrate?

(*Dr Fisk*) The general thrust, my Lord Chairman, is that if there is a hazardous effect associated with the release of a genetically modified organism, its risk is that it is potentially self-replicating. This makes it substantially different from the risk that one might have had from a chemical hazard which would otherwise be localised or require other means of transportation. That is the main thrust of the risk that we should look at, the mechanisms of transfer and the degree to which it can be moved into other replicating organisms. I do not know whether Dr Gillespie would like to add any more, my Lord Chairman.

(*Dr Gillespie*) My Lord Chairman, certainly there are a number of examples where there is an unexpected new combination of genes, and I can give you as a good example of this, *Spartina anglica*, where unexpected new combinations have quite a significant effect on the environment. *Spartina* is in fact a hybrid of a grass. Unexpectedly it is able to colonise inter-tidal zones and it has become quite a problem, particularly in Welsh harbours. We should say that from a risk assessment it would be difficult, unless thinking quite laterally, to predict that this effect would in fact take place. It is this sort of unexpected effect that was emphasised by the RCEP in their 13th and 14th reports. But specifically we are most concerned about genetically modified organisms.

67. What you might call monster plants, I suppose?

(*Dr Gillespie*) I am not quite sure that I should call *Spartina* a monster plant, my Lord Chairman. Others, of course, have used it in reed beds for sewage filtering, so there are pluses and minuses in this particular example.

Lord Soulsby of Swaffham Prior

68. I was just wondering how far your interest or authority extended. I can see the environment generally defined as the wild plants and animals and what we consider to be the environment, but where do domesticated plants and domesticated animals come into this? Are you responsible for cattle, sheep, farm animals? Do you control that, or is that the Health and Safety Executive which would do that?

(*Dr Marquard*) My Lord Chairman, part VI of the Environmental Protection Act defines the environment as being land, air and water, and goes on to talk about damage to the environment being damage caused by organisms in the environment or supported by the environment, so in essence as far as genetically modified organisms are concerned our responsibilities would extend to domesticated animals but only as far as the genetically modified aspects are concerned, not as far as the normal responsibilities covered by the Ministry of Agriculture are concerned.

Lord Gregson] So you say that you are cutting across the traditional lines of responsibility in effect?

Lord Walton of Detchant

69. So that the effects of contaminated foodstuffs in farm animals would fall clearly to the Ministry of Agriculture, Fisheries and Food and would not be your responsibility at all?

(*Dr Fisk*) That would be my understanding.

Lord Soulsby of Swaffham Prior

70. If I may just follow up on that, my Lord Chairman, while that is fairly clearly defined there are areas of course where the borders are rather fuzzy and it may well be that the Ministry of Agriculture does not know what its full responsibilities are with farm animals or with wild animals that come into contact with domestic species either naturally or in a cultivated way. Who handles that side of the issue? Is it all MAFF people who do that or would you come into it in your earth, air and water aspect?

(*Dr Fisk*) My Lord Chairman, perhaps it would be helpful if Dr Marquard explained a little how the advisory committee works becuase this is the network by which all aspects that must be taken into consideration initially are brought to one point.

(*Dr Marquard*) The advisory committee consists of scientific experts and representatives from both sides of industry, environmental groups, and very importantly we have assessor positions for all the relevant departments. This means that as soon as we receive an application for a consent to release all other departments receive copies of those papers. This allows them already to start their own scrutiny and if there are any aspects that they consider would fall within their responsibilities it allows them to take that up. This has been very clearly set out in the memorandum of understanding to which the Health and Safety Executive referred when they were giving evidence earlier and we have been operating a system like this for a number of years and have found that it works very smoothly. The memorandum of understanding now provides a framework within the new legislative structure for ensuring that there is harmonised approach and good contact between departments.

Chairman

71. Our attention has been drawn to an ACOST report, Developments in Biotechnology, 1990, which recommended that the Department of the Environment fully consider the applications of biotechnology to the environment, including beneficial aspects, and convey the results of their assessments to the public. What have you done about that?

(*Dr Fisk*) My Lord Chairman, the department has recognised from the outset that this technology, particularly the new genetically modified organism technology, offers really substantial gains for some areas of environmental policy. Technology is much broader, of course, than what one might call "green" genetically modified organisms, but "green" GMOs have a very important part to play. The department jointly funds with the Department of Trade and

[Chairman *contd.*]

Industry a scheme called the Environmental Technology Innovation Scheme. That that scheme already has one particular application of biotechnology. It is part funded with industry. But we also recognise in the October 1992 white paper that within the range of genetically modified organism proposals that we were receiving for release there were indeed some that were environmentally benign and, indeed, positively helpful to the environment. Therefore, the white paper laid out a proposal by the Government that we should as far as possible accelerate the process by which these were approved. It seemed to us that this was a very logical step to be taken. We believe that we are the first Member State of the European Community to take this step of having a faster green track. These were just two of the steps that we had, my Lord Chairman. We are very conscious that the industry itself is making an excellent job in promoting some of the more environmentally friendly aspects of biotechnology, but, of course, we are still some way away from marketable products in many of these areas.

72. Now you have had a number of proposals, I gather. How many consents have you given and what response have you had in relation to these from the public?

(*Dr Marquard*) My Lord Chairman, the regulations came into force, as you know, on the 1st February of this year. Since the 1st February we have received seven applications for consents to release. We have not as yet issued a consent, but expect to do so in the very near future.

73. That seems quite reasonable. We had some discussion earlier this morning about the question of vertical and horizontal regulations. Have you any views on this as to which is preferable?

(*Dr Fisk*) My Lord Chairman, I think that we should take the very strong view that differentiation between horizontal and vertical is academic if the regulations are risk based, and that is actually the approach that most regulators in most developed countries have taken. A regulator in assessing the risk of a genetically modified organism release must take into account all the available information. If some information relates to the fact that it is to be used as a product or in another case that it is to be used in many different ways these are the issues that will be taken into account. In our view the role of horizontal versus vertical is more to do with the efficiency of the regulatory process and its ability to deliver safe regulation. A simple example would be that in cases where a genetically modified organism was going to be used as a very specific, well defined product with a specific use. Taking this into account will influence the way in which the risk assessment was made. There are other cases such as research and development release in which it would be really burdensome actually to have to look at whether this release met the criteria of bio-pesticides release, the plant products releases and so on. The worst case, the one that we would very strongly wish the United Kingdom to avoid, would be one where we applied horizontal and vertical requirements together, which cause unnecessary complexity.

74. Did the same thing, you mean?

(*Dr Fisk*) Yes, did the same thing. This appears to be the cause of some concern in the United States in the complexity of their own regulations. We do know that some industrialists in the United States have pointed out that in Europe there is effectively a one stop shop in terms of getting releases approved and that is not true for some products in the United States where simply by legal definition a particular genetically modified organism may appear to be more than one type of product and therefore addressed by more than one vertical stream of regulation. In some cases at state level, because there is mixed competence between in Federal Government and individual states, some states have already imposed a horizontal control as well as the vertical control on products. Our American colleagues are putting as much energy to improve the efficiency and movement of their regulations in this area as we are and I am sure that these problems will not persist. However, it is a lesson that we must learn, that there are·attractions of vertical and horizontal approaches properly applied but not when applied simultaneously. The United Kingdom has taken the view that general product regulations, particularly for this new area of technology which promises so much, really must have the flexibility to include genetically modified organism products in their format. Fortunately the European Community directive on deliberate release provides that mechanism and we are up to at least political agreement on the first product directive that will contain the necesary risk assessments to include the release of the genetically modified organisms. So we are making progress. It would be true to say my Lord Chairman, that some of those who have argued for vertical regulation had perhaps a more cosmetic rather than administrative efficiency view point. That is they would rather have the product seen as a tomato than as a genetically modified tomato. But looking at vertical regulation systems where they have been applied, it is still necessary for the regulator to take into account all the information that he has, and this includes the genetically modified origin. Very naturally there is a slight bifurcation in the vertical regulatory system. The most obvious example, my Lord Chairman, is in the United States Environmental Protection Agency where pesticides are treated as a product but there is a special route which handles those that have a genetically modified organism origin. It seems to me a very defensible process. It is still an efficient way of handling biopesticides, but it is not just a matter of presentation; it is a matter of administrative efficiency.

75. But we believe that the industry is inclined to complain a bit about the regulatory system here in Britain. Are you aware of this? Do they complain to you, or do they just complaint to us!

(*Dr Fisk*) Industry, of course, has been very closely consulted right from the beginning of the European Community directives, my Lord Chairman. Indeed, industry were quite right to say that a growing diversity of approach in different Member States made a very strong reason why the Community had to act at the internal market level to get some

[Chairman *contd.*]

uniformity. There was, of course, a considerable consultation and input in evidence to the Royal Commission on Environmental Polllution before they put forward their own recommendations. Our own regulations I think have benefited from some of the most extensive consultations that we have conducted for some while. Indeed, the change between our early draft and our later drafts shows that we did try to take on board all the issues that industry raised. We are keen to see any issue raised in the course of this enquiry which we can take forward. From my own department's point of view, my Lord Chairman, when the National Economic Development Office issued a report on biotechnology not long ago it did reserve a section for regulation—some of the points that you made were made in that report—and we took the initiative immediately to invite NEDO to have a small subgroup to look at the performance of regulation in this area. We were as keen as others to make sure that all the data that were available on the relative performance of regulations were in the public domain, and we were not trading in mythology. Of course, one always thinks that the regulatory grass is greener in the other valley. I think that that was a very helpful group. With the demise of NEDO chairmanship will now be taken over by, or rather, is taken over by, my colleagues in the Department of Trade and Industry and we hope to play an active part in that process. I just wondered therefore, my Lord Chairman, whether it might be helpful if I were to flag up what I believe were the three areas that arose most in consultation.

76. Yes, please, Dr Fisk?

(*Dr Fisk*) I guess that I can summarise them as three, the fees and charges system, the information requirements that we impose on industry before consent and the performance of the public register of information. In two of those I do not think that the department would want to offer any excuses. The fees and charges system is our system for recovering the cost of running the scheme and we believe it is right that the industry and not the taxpayer in general should fund it. The public register of information in our view is an important part of gaining public confidence and, indeed, has to meet the requirements under the access to information directive. As to the information requirements, my Lord Chairman, this is an area in which we are continually working with industry and with our colleagues in Europe because as experience is gained in this area we require less information as we have more confidence in the performance of certain categories of genetically modified organism release. We rather hope the Government's announcement in the October 1992 white paper indicates that we are attempting to be flexible in that area. But at the moment, my Lord Chairman, we believe that we have the right level of information coming in although we are looking for ways in which it can be progressed forward within the context of this being a European directive.

Lord Gregson

77. My Lord Chairman, may I ask the question that nobody wants to ask on this subject, and it is this. There is an enormous commercial advantage to be gained by a country from biotechnology research and you must be aware that there is a very unofficial league table of countries in which it is desirable to carry out that research. The real problem of course is that it is a bit like a football league. Countries are vying with each other to suck in this type of activity. You must be aware of this, and we must be very careful, must we not because the level playing field is on an international basis, not on a Community basis?

(*Dr Fisk*) There are two points here, my Lord Chairman. The first is that the enormous potential for wealth creation that Lord Gregson has referred to clearly applies to products, and the view we have taken is that the enormous internal market for European products meant that we had to have the internal market regulated. It would be true, that as far as some countries within Europe were concerned their public—not just their regulators—were more wary of this technology than others and therefore that it has been a very important part of the role of the European negotiations to produce, a level playing field; and to provide access for products produced in this country throughout Europe so that we do not, as it were, find ourselves tripping over new and difficult regulatory barriers. That is very important it seems to me for the market. Secondly, we are already working through the OECD on a series of very important guidelines to try to harmonise the way in which regulatory procedures are going to go forward in the developed world. As I indicated earlier, my Lord Chairman, because many of these approaches are risk based I have a great optimism that we will actually have some uniformity within this area. One of the slighty different characteristics of genetically modified organism technology, I should guess, is that it does not necessarily require the vast capital investment of some other advantaged technologies. Therefore, we are talking about a wider world than just OECD for this technology. This department recognised that very early on during the preparations for the United Nations Conference on Environment and Development that took place in Rio in June of last year. The United Kingdom with our colleagues in the Netherlands took a very strong lead to attempt to lay out some principles in Agenda 21 which might underlie the possible use of biotechnology world wide. I think it is no secret, my Lord Chairman, that the United Kingdom felt that we did not make as much progress as we should have liked, but we did make some progress. Indeed, one of the international conventions that were signed at that time already has a reference to possible protocols in this area. Our view therefore is that everybody has an interest in a level playing field for the access of products and that is important, and was clearly keen that there are as equitable as possible guidelines for research and development. This is not only for the reasons that Lord Gregson referenced but another concern that the regulator must have. It is that very often countries with very sensible, level-headed, businesslike regulations can find that an accident through foolish and stupid regulations elsewhere can contaminate the whole public debate in the area in which we are working. We are therefore very keen to ensure that some of the rapidly developing countries are brought into this debate on what are the appropriate guidelines and processes.

[Lord Gregson *contd.*]

78. It would be almost inconceivable if someone in Timbuktu or suchlike developed a cure for Alzheimer's disease and found that national boundaries stopped the product going out of the country—there would be demonstrations in the street and hanging from lamp posts and so on, would there not? It is inconceivable, is it not, to think that you could stem the tide of this sort of development by regulation or boundary control?

(*Dr Fisk*) My Lord Chairman, I suspect that I am being invited to make suppositions that I am probably not qualified to do!

Chairman

79. In your written evidence at paragraph 35 you talk about the deliberate release directive and you speak of the one key, one door approach. That is not a phrase that I am immediately familiar with. I wonder whether you could tell me what it means?

(*Dr Marquard*) My Lord Chairman, it is a driving towards the vertical legislation that has been referred to in the discussions this morning. It is to try to obviate a dual regulation of biotechnology products so that as soon as a product has gone through its development it is taken out of the horizontal regulatory scheme and moves into the vertical scheme so that there is just the one door and the one key.[1]

80. Good—I think I will read that when the evidence comes out! In relation to the single key, single door the United Kingdom, which presumably means this department, has been pressing for the line of action that you have just outlined to me. How are you getting on with that? Is your pressing successful?

(*Dr Marquard*) My Lord Chairman, in fact not only are the Department of the Environment concerned, but the product regulation negotiations are usually conducted by other departments. For example, the Medicines Control Agency is responsible for the negotiations on the human and veterinary products regulation, the Ministry of Ariculture is responsible for the plant protection products directive and so on, but because of the very good contacts between the different departments we are putting to colleagues who are negotiating those directives and regulations the need to take into account the risk assessment contained in the deliberate release directive to ensure that that is carried through to the product regulation so that it [the product] can then be taken out of the horizontal deliberate release directive.

81. Do I understand then that your departmental pressure is not directly to Brussels but indirectly through other parts of what we might call Whitehall?

(*Dr Marquard*) The department, in attending the competent authorities meetings for 90/220 certainly always asks the Commission for an update on progress in product directives/product regulations. The derogation from the deliberate release directive only takes place with the vote of the competent authorities for that directive so that the requirement for horizontal regulation is only removed once the competent authorities for 90/220 have taken a positive decision that that derogation is appropriate. It is important therefore I think from both aspects that we do have an input as the Department of the Environment as the lead department for 90/220 and Brussels that way and through colleagues negotiating other directives with other directors general in the Commission.

Lord Gregson

82. My Lord Chairman, considering the problems that have arisen from insurance for contaminated land (a saga that has been going on for about 14 years to my knowledge and I do not think there is any real resolution to it) is somebody in Government—it may not be you but perhaps the Department of Trade and Industry—talking to the insurance industry about product liability in this field?

(*Dr Fisk*) My Lord Chairman, the Environmental Protection Act does indeed place on those who would be responsible for release which proved to cause harm the possibility that they may be required to fund a clean up. That is part of the structure.

83. The polluter pays?

(*Dr Fisk*) The polluter pays, yes. Indeed, with reference back to the case of the renegade grass which is very gradually working its way into waterways, such clean ups could be very expensive. It is my impression that the American insurance industry is possibly more alive to this issue in their relationships with a number of key companies than the United Kingdom sector. We have not ourselves as a department had close discussions with the United Kingdom insurers.

84. You have, however, on contaminated land?

(*Dr Fisk*) We have, yes.

85. Is there any reason why you should not have carried that sort of discussion on, or is it because the Department of Trade and Industry and several other ministries are involved at this stage?

(*Dr Fisk*) The issue of contaminated land, of course, my Lord Chairman, is one where the contamination is there and it is an issue clearly of risk, a very real and exposed risk.

86. Or might be contaminated in the future? It is not necessarily a closed subject, in fact?

(*Dr Fisk*) But, as Helen Marquard has described, given the present state of the number of releases that have occurred in the United Kingdom it would be a little difficult to put genetically modified organism releases in quite that same class. I should also add, of course, that it is very clear from the industry's point of view that the very last thing that they wish to get into is the particular case of contamination or damage. They are as keen as we are for this risk to be as minimal as, indeed, the law requires it to be. That would be my apologia for why we have not, as it were, led on the insurance issue, because we rather hope that the insurance companies will be persuaded that the regulatory approach and in particular the way in which we look at consents, satisfies them that the risks are, indeed, very insurable.

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[1] Note by the witness

Chairman

87. Unless my colleagues have any further questions to ask I should like to ask one last question. I gather that there is to be an environmental agency of some sort set up presumably in the near future. What is it intended to achieve in your field of activity? How will you be related to this new agency? How will other departments be related? Or do you not know yet?

(*Dr Fisk*) My Lord Chairman, the decisions on the location of the work of the control of genetically modified organisms in relation to the future of the agency have not yet been taken. I think that one would view that as premature. It is very clear that the key impetus of the agency is to bring together the existing main regulatory structures, the National Rivers Authority, the waste regulation authorities and Her Majesty's Inspectorate of Pollution, and all three of those do not form part of the present regulatory structure on genetically modified organisms or, indeed, on chemicals or pesticides, but clearly one has to keep open for review what would be the best and most efficient regulatory structure in the future. Within our own genetically modified organism system at the moment, for example, field enforcement is actually undertaken for us under contract by the Health and Safety Executive, which in our view is one of the most efficient ways of ensuring that users are not bothered by more than one inspectorate turning up essentially to look at the same product and process. Our main aim therefore must be for regulatory efficiency and minimum burden.

88. You would expect perhaps the new agency to proceed in a somewhat similar manner, would you, that is, by devolving the inspection to some other body, or would it in fact set up an inspectorate of its own?

(*Dr Fisk*) My Lord Chairman, perhaps I did not express myself clearly there. At the present time we have no specific plans for the control of genetically modified organisms moving away from the present position in the department. I simply pointed out, my Lord Chairman, that of course the regulatory position on the agency must be an evolving one.

Lord Gregson

89. It could, of course, have an effect on all the agencies, more directly probably, the National Rivers Authority, which goes back to the organising body needing necessarily to be part of the regulation equipment of the new protection agency?

(*Dr Fisk*) My Lord Chairman, as I said, I think that some of these issues would be viewed by the department as premature at this stage.

Chairman] Thank you very much, Dr Fisk. If you want to amend or to clarify your evidence in any way, please write to us and let us know. Thank you very much for coming.

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HOUSE OF LORDS SESSION 1992-93

MINUTES OF EVIDENCE
TAKEN BEFORE

THE SELECT COMMITTEE ON SCIENCE AND TECHNOLOGY

(SUB-COMMITTEE II REGULATION OF THE UK BIOTECHNOLOGY INDUSTRY AND GLOBAL COMPETITIVENESS)

Thursday 25 March 1993

DEPARTMENT OF TRADE AND INDUSTRY
Dr E Finner, Dr E Baker and Mr C Hoptroff

MINISTRY OF AGRICULTURE AND FISHERIES AND FOOD
Mr P Murphy and Mr J Bainton

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THURSDAY 25 MARCH 1993

Present:

Flowers, L.	Renwick, L.
Gregson, L.	Soulsby of Swaffham Prior, L.
Howie of Troon, L. (Chairman)	Wade of Chorlton, L.
Kennet, L.	Walton of Detchant, L.
Perry of Walton, L.	Whaddon, L.
Platt of Writtle, B.	

Written evidence from the Department of Trade and Industry

Question 1: What is your interest in Biotechnology?

1. Biotechnology has far-reaching implications for the UK economy. Because of its industrial significance, DTI aims to champion the commercial exploitation of biotechnology in the UK.

2. Other departments have lead responsibility for a number of aspects of Government policy which affect industrial competitiveness, including regulation of biotechnology. DTI has an interest in the impact of those policies on the competitive position of UK industry.

3. DTI supports industrially relevant research and the transfer of technology through the LINK and Eureka schemes and the industrial awareness campaign *Biotechnology Means Business.*

4. DTI is the lead department on intellectual property and has responsibility for regulation in this area, where there are key issues affecting biotechnology.

Question 2: How and why is biotechnology important to UK industry?

5. Biotechnology is a key enabling technology for several sectors of major importance to the UK economy, in particular healthcare, chemicals, agriculture, food and environmental remediation.

6. In 1991, the latest year for which figures are available, NEDO estimated UK-originated biotechnology products and services to be worth about £366 million with almost 50 per cent exported, and 5,000 people employed. The US is world leader with some 24,000 employees, and the UK is among the second-order players, behind the US and Japan but matching Germany and France.

7. Biotechnology is not the only factor that will determine the competitiveness of its user sectors, and neither is it likely to become so. The usual range of determinants such as quality, management, innovation, production efficiency, skills and marketing will remain as relevant as ever. Nonetheless, the importance of biotechnology is growing.

HEALTHCARE

8. In 1992, the UK pharmaceuticals industry was estimated to have recorded a trade surplus of £1.3bn, and was the UK's third largest net exporting sector. Employment was about 81,000, including a high proportion of scientific and technical manpower. The pharmaceuticals sector has the largest civil industrial R&D spend in the UK (about £1.2bn in 1992).

9. All of the major UK pharmaceutical companies have significant activities in biotechnology and its importance is growing. Many of the newer biotechnology-centred companies in the UK are also based on human therapeutics.

10. In the other main healthcare sector, diagnostics, the UK is not at present a major world player despite a strong science base. Nonetheless, the market is changing rapidly and the UK has the opportunity of using its scientific potential in biotechnology to develop a stronger position.

CHEMICALS

11. Chemicals (other than pharmaceuticals) showed a positive trade balance of about £1.3bn in 1991.

12. The chemicals industry has been involved in the development of biotechnology from the beginning. The Senior Advisory Group Biotechnology (SAGB), which represents several leading European companies active in biotechnology, estimated that the world market for biotechnology based industrial chemical products would increase from £70m to £10.4bn between 1990 and 2000. Whilst this figure is no more than an approximation, it reflects industry's expectations of very rapid growth of biotechnological processes in this sector and their importance to future competitiveness.

THE FOOD CHAIN

13. Despite many strengths in agriculture and food and drink manufacture, the UK runs a significant overall food and drink trade gap. Biotechnology offers one means of strengthening our competitive position.

14. Biotechnology can help increase efficiency, particularly of food processing, and offers the possibility of reducing use of pesticides and fertilisers. The food and drink industry will be affected by new agricultural products as well as improved flavours and reduction of naturally-occurring harmful ingredients. The introduction of new diagnostic tests will improve food safety.

ENVIRONMENTAL REMEDIATION

15. Biotechnology will enable many novel kinds of environmental management, saving costs and generating new value. The main areas of development are expected to be use of biological processes to cut industrial pollution; improved techniques for hazardous waste management; biodegradable plastics and reduced agricultural waste.

Question 3: What future prospects and opportunities does the technology offer?

16. The starting point for assessing future trends is statistics relating to present output, and here the latest figures are from the early 1990s. Among the principal estimates are the following:

- SAGB estimate the current world market for biotechnology products at some £3.6bn.
- The US President's Council on Competitiveness report of 1991 estimated the current US market at £1.1bn.
- County Natwest estimated world sales of six key therapeutic proteins, such as hepatitis B vaccine, to be £1.34bn in 1990.
- A NEDO survey in 1991 estimated UK biotechnology product sales at £250m, increasing to £350m in 1991.

17. These estimates are broadly compatible, and offer a baseline for estimates of future development.

18. The statistics also demonstrate significant growth. The NEDO survey, for example, showed an increase in sales of products and services related to what was termed the 'new' biotechnology of 23 per cent in 1989, 25 per cent in 1990 and 42 per cent in 1991.

19. For the future, SAGB forecast a growth rate of 30 per cent compound to 2000, and the US President's Council on Competitiveness forecast a compound growth rate of nearly 40 per cent to 2000. For such growth rates to be achieved, a number of things need to happen, and many of these are outlined in the answer to question 12.

Question 4: Which developments in biotechnology raise issues of safety and how should they be addressed?

20. Specific safety implications of biotechnology for workers in the workplace and for the environment are regulated by HSE and DoE respectively and addressed in their evidence.

21. Where issues of safety arise, it is important for public confidence that regulation takes due account of the risk involved. Balanced regulation also serves the interests of those wishing to develop new products or processes, which will only be successful in the market place if they have the confidence of the public.

22. The regulatory framework should be founded on sound science and sensitive to public concerns. Assessment of the degree of risk is fundamental.

Question 5: Should biotechnology be regulated by an industry specific regime?

Question 6: From a technical point of view, is horizontal regulation (where a product is judged through the process by which it is derived) better than vertical regulation (where a product is judged by its characteristics)?

Question 7: Should regulation evolve from a horizontal to a vertical approach in each industrial or environmental application?

23. Biotechnology is not itself a discrete industry; rather the term embraces a set of enabling technologies. Its techniques are being applied by several industrial sectors and are therefore already subject to all pre-existing regulations controlling those industries.

24. In response to perceived public concern, an additional range of regulations has been developed dealing with the contained use of genetically modified organisms and their deliberate release into the environment.

25. Where biotechnology raises issues which are not industry-specific, then horizontal regulation may be appropriate. However, where it forms the essence of an industry-specific process or product, then industry-specific regulation may be better.

26. The Government's policy is to avoid unnecessary or overburdensome regulation (*Releasing Enterprise* (Cm 512, November 1988)) and this approach has recently been reinforced by the Prime Minister's initiative on deregulation. Against this background it is particularly important that firms should not be faced with unnecessary duplication of testing and authorisation procedures, which incur additional costs without any additional benefit for the consumer. The relationship between horizontal and vertical regulation is therefore vital: it is important that procedures are streamlined so that one assessment and notification procedure covers all that is required for product authorisation.

Question 8: How do current regulations compare with those of other competitor countries?

— *In Europe*

— *In the Far East*

— *In the USA?*

27. In the EC, directives EC/90/219 covering contained use and EC/90/220 covering deliberate release provide the basis for a consistent regulatory regime. However, not all Member States have yet implemented these directives. Only when measures have been fully implemented throughout the Community and experience gained on their application will it be possible to estimate how far a consistent regime has been achieved in practice.

28. In its 1991 communication *Promoting the Competitive Environment for the Industrial Activities Based on Biotechnology within the Community,* (SEC(91)629 final, 19 April 1991) the European Commission acknowledges the need to promote the beneficial application of biotechnology and to avoid creating undue burdens for industry, while of course ensuring safety for man and the environment. The communication sets out recommendations for future Community Policy, which were endorsed by the Council of Ministers on 17 November 1991. The Commission has established the Biotechnology Coordination Committee (BCC), a high-level, inter-service committee, chaired by the Secretary-General to the Commission, to coordinate activity, taking account of the various interests at stake, and to pursue implementation of this framework.

29. We know of no authoritative comparison of the regulatory framework in Europe, the US and the Far East. However the European Commission has some work in progress on comparing the US with Europe, and towards the end of 1992 released for consultation an interim report, *Regulatory Framework and Research Policy Effort on Biotechnology in the EC and the US*. This concluded that, at the pre-marketing stage, there is more flexibility in the US, but that required risk assessments seem to be broadly comparable in terms of information requirment and administrative burden.

Q9. What are the consequences, or likely consequences, of the regulatory regime on competitiveness of UK industry, in particular as regards

(1) Research

(2) Product development

(3) Investment

(4) Location

(5) Sales and marketing?

30. A cluster of mutually-reinforcing factors needs to be present in order for a particular country or region to build up a competitive advantage in a given industrial technology. It is rarely meaningful to isolate one part of the industrial process and concentrate on it to the exclusion of others. The regulatory regime will impact on all of the areas specified in the question, but in different ways at different times: furthermore, it will be only one factor among many influencing industrial competitiveness.

31. Key elements of the UK regulatory regime have only recently come into force and it is therefore too soon to say what effects, if any, the regime will have on aspects of UK competitiveness. We will, however, be monitoring developments carefully.

32. The UK's research effort is an important source of competitive advantage, and clearly its development over the last decade has not been impaired by regulation.

33. There are concerns on the part of UK industry that the field release approval system in the EC will prove more onerous and protracted than that in the US. Experience will show whether this is the case, but the simplified approval procedures for release which are under development in Europe will undoubtedly help.

Q10. Is there a danger that the present regulatory regime will prevent the exploitation by British industry of the research conducted in the UK science base?

34. The UK science base in biotechnology is strong, and British industry has made good use of it. The impact of the new regulatory regime will not be clear until the new regulations have been in force for some time. We will be monitoring developments closely, including administative burdens and the extent to which difficulties arise over commercially confidential information.

Q11. How best can issues of public acceptance be addressed?

35. Winning acceptance of particular products from consumers is largely a matter for the companies concerned. An open, straightforward stance by industry will do much to influence public confidence.

36. The regulatory framework plays a part in ensuring that products are safe, efficacious and of satisfactory quality, and contributes to public confidence. Regulations should be soundly based on science and sensitive to public concern.

Q12. What other factors do you consider will play a crucial role in the competitiveness of the UK biotechnology industry?

37. Regulation is only one factor determining industrial competitiveness in biotechnology. There are others, and these are discussed below.

The Science Base and Technology Transfer

38. A prerequisite for effective technology transfer is a secure system for the protection of intellectual property rights. As noted below, the EC Directive on the Legal Protection of Biotechnological Inventions is still some way from fruition, and in the meantime a number of issues surround the patenting regime.

39. The Government operates a range of initiatives in biotechnology. There are currently 12 LINK schemes in this area with a £100m total budget, of which the DTI commitment is some £30m. *The Biotechnology Means Business* awareness programme has now reached 500 small and medium-sized firms in a range of industrial sectors.

Public Perception

40. As mentioned in the answer to question 11, public acceptability will be a key factor in the development of biotechnology-based processes and products in the UK.

Capital Investment

41. Capital and R&D investment requirements in much of biotechnology are high—typically 10 to 20 times more than for manufacturing in general. Second-round funds will typically last only 2 to 3 years in a 5 to 10 year development plan. Most biotechnology companies will therefore need a heavy third round of financing before reaching the commercial stage of product development. Raising such funds has proved difficult for some biotechology companies.

Manpower

42. The availability of qualified scientific manpower will be vital for the commercial take-up of biotechnology by British industry, particularly as larger-scale production takes over.

Intellectual Property Rights

43. There are key intellectual property rights issues to be resolved in biotechnology, and these stem from the particular nature of the technology.

44. Biotechnological products are different from other inventions because they may be self-reproducible. The extent to which such reproduction in the hands of a user is an infringement, and in particular the extent to which a farmer may save seed of patented plants to resow on his own land the following year, has to be clarified.

45. At present, it it not possible to patent plant varieties as such, and many in industry would like to see this exclusion removed in order to stimulate research. Nonetheless, a plant variety which is the subject of plant breeders' rights may incorporate patented features: this raises the question of whether, and if so under what conditions, the holder of a plant variety right should be able to compel a patentee to grant a licence under a patent without which the variety cannot be commercialised.

46. Another area of debate is how far the grant of patents for, for example, transgenic animals should be restricted on ethical grounds. Patent offices are not well placed to decide these ethical issues and it would be better for them to be dealt with in other ways and patents granted for the results of any legitimate research.

47. Biotechnological inventions are special in that it is often not possible to give a full description of the invention without making a sample of biological material available. This has led to applicants for patents depositing the material in culture collections. The Budapest Treaty has simplified this process by providing for the international recognition of culture collections as depositary authorities. However, not all countries, even in the EC, are signatories to the Treaty. Industry is concerned because in some countries, samples of the deposit have to be released to third parties before they are assured of a patent. In the UK, this has been dealt

with by allowing applicants, in the period between publication of the application and grant of the patent, to restrict the release only to independent experts and not to direct competitors of the patentee.

48. These issues remain are being addressed in the EC draft Directive on the Legal Protection of Biotechnological Inventions.

Chemicals and Biotechnology Division
Department of Trade and Industry
151 Buckingham Palace Road
London SW1W 9SS

22 March 1993

Examination of witnesses

Dr E G Finer, Head of Chemicals and Biotechnology Division, Dr E Baker, Chemicals and Biotechnology Division, Dr P Baker, Laboratory of the Government Chemist, and Mr C Hoptroff, Principal Examiner, Intellectual Property Policy Directorate, Patent Office, Department of Trade and Industry, called in and examined.

Chairman

90. Dr Finer, thank you for coming. Would you please introduce your colleagues, just say a little about the background and then, if you wish, give us a general account of where you think we now are?

(*Dr Finer*) Thank you, my Lord Chairman. Dr Elizabeth Baker is the head of the biotechnology branch in my division, that is, the Chemicals and Biotechnology Division of the Department of Trade and Industry. Dr Peter Baker (unrelated) is head of Food and Bioscience Division at the Laboratory of the Government Chemist, which is a Department of Trade and Industry executive agency, and he provides us with help on the biotechnology regulation side. Mr Cedric Hoptroff is from the Patent Office and it is in the area of intellectual property rights that the Department of Trade and Industry exercises its main regulatory function relevant to biotechnology. Mr Hoptroff will therefore try to answer any questions the Committee may have on that subject. Unlike Liz Baker and me, Peter Baker has several years' experience in biotechnology in government so I hope that he will also be of value to you. My and Liz Baker's involvement stems from last summer when the President of the Board of Trade reorganised the Department of Trade and Industry and among other things he set up several new sectoral divisions. The Chemicals and Biotechnology Division was one of those, my Lord Chairman, and I was asked to head it. The Department of Trade and Industry had been active in biotechnology for about ten years before that through the Biotechnology Unit, which was, and still is, based at the Laboratory of the Government Chemist at Teddington. That unit itself dealt mainly with technical issues and issues related to technical subjects. During that period biotechnology has evolved from a virtually solely research based technology to an area much nearer the market, and that change was reflected in the formation of my division with new policy responsibilities for technology. The old Biotechnology Unit at Teddington still exists and, indeed, has been beefed up and it is now part of Liz Baker's branch; and in addition she has a policy section based up in Victoria. I will come back to that if I may later, my Lord Chairman. We have therefore been in existence for about six months and over that six month period we have been bringing ourselves up to speed. Our aim has been to get to know some of the key sectors, develop an understanding of the problems and start to tackle some of the issues which have been raised with us. The objective underlying the whole thing has been to promote United Kingdom industrial competitiveness in biotechnology issues. We believe that biotechnology will not have a future unless the public has confidence in products and processes using it. A sensible regulatory framework is an integral part of establishing and maintaining public confidence so the Department of Trade and Industry and the regulatory departments have common objectives in wanting such a regulatory framework. Our job in the Department of Trade and Industry is to work with the regulatory departments to ensure that the industrial competitiveness dimension is fully born in mind as regulatory frameworks and regulations are developed here in the United Kingdom and in the European Community and, indeed, anywhere else such as other international fora. We are bringing the industrial dimension into biotechnology regulation in two ways. First of all, my Lord Chairman, we have formed a committee called Biotechnology Industry Government Regulatory Advisory Group.

91. I am glad you have come to that, Dr Finer—we wondered what BIGRAG was!

(*Dr Finer*) I am sorry about the acronym, my Lord Chairman, but at least one can say it! As I think that you may know, my Lord Chairman, the Biotechnology Industry Government Regulatory Advisory Group, BIGRAG, is a successor to a NEDO committee, which performed a very similar purpose. The terms of reference of the biotechnology industry government regulatory advisory group are broadly to advise Government on biotechnology from the industry point of view. That is one of the ways. The other way is that the Cabinet Office has formed a new committee at official level to bring together relevant departments to discuss policy on regulatory issues. We have also been concerning ourselves, of course, with non regulatory issues relating to industrial competitiveness in

[Chairman *contd.*]

biotechnology. The first among these has been technology development and technology transfer where the work of the Biotechnology Unit has carried on and, indeed, expanded. On the technology side, my Lord Chairman, we are fortunate in that there is a senior and well respected committee called Biotechnology Joint Advisory Board, BJAB, which is chaired by an industrialist at present, Dr Ed Dart from Zeneca, and industrial and academic practitioners sit on that board. The Biotechnology Joint Advisory Board provides advice to all the research councils and to us in the Department of Trade and Industry, and we in DTI provide the secretariat. Finally, other areas in which we have been active include the investigation in detail of the problems to do with the availability of finance for small biotechnology companies with a view to deciding on the scope for action, looking at intellectual property issues, which are very important in this area, and considering what if anything could be done to improve the public perception of biotechnology, again a key question, my Lord Chairman, and, of course, I should be happy to expand on those later if you so wish.

92. Thank you very much. I notice from information that we have had from you, Dr Finer, that the Department of Trade and Industry is the lead department in intellectual property, and we will be coming to that a little later on, and that other departments lead in a variety of other ways. How is this co-ordinated? How in fact determines the central policy, assuming that there is one?

(*Dr Finer*) My Lord Chairman, like other areas in government, for example, if we think of chemistry, biotechnology impinges on a number of policy areas and in each case the department that has the key responsibility for the policy area takes the lead and as always in government consults other interested departments, but overall responsibility for co-ordination rests with the Cabinet Office. The Cabinet Office has recently established a committee called the Interdepartment Group on Genetic Modification Technology, which brings together departments with an interest in these areas so the Cabinet Office has the overall key co-ordination role. We ourselves take a co-ordination role in the area covered by the Biotechnology Joint Advisory Board where the science interest is brought together to match the interest of industry. I should see the Department of Trade and Industry having a key co-ordination role there.

93. You seem to describe a series of interlocking circles?

(*Dr Finer*) I am afraid that that is the way it is, yes, my Lord Chairman, but I think that that is inevitable with any technology or science that covers such a wide range of interests as biotechnology does.

94. You mentioned the cabinet committee. Is it the business of the cabinet committee to pull these circles together?

(*Dr Finer*) Yes, my Lord Chairman. For example, when there are issues where we might have to agree a negotiating stance in the European Community or a line to take when visiting an OECD meeting that is the sort of area when the cabinet committee will play a role.

Chairman] Can you tell us who sits on it, Dr Finer?

Lord Gregson

95. It is published, is it not?

(*Dr E Baker*) My Lord Chairman, the departments who have regulatory interests are represented on that committee as are the Scottish Office, the Welsh Office and the Northern Ireland Office, and there will be a research council representative as well as Department of Trade and Industry representation, and the chair is taken by the Office of Science and Technology for the Cabinet Office.

Chairman

96. We have heard a good deal about regulation, which you have mentioned yourself. To what extent is there a conflict between regulation and competitiveness? At the same time I notice that somewhere in your submission you talk about the danger of over regulating. Is there also a danger about under regulating?

(*Dr Finer*) My Lord Chairman, as I said, for industry to succeed it is vital that consumers have confidence in the products and in the processes that are used to make the products, and we believe that that confidence requires a proper regulatory framework, but it is the Government's clear policy to avoid unnecessary and overburdensome regulation. The specific purpose of that is to ensure that industry's competitiveness is not adversely affected. Therefore, we see the need for competitiveness and the need for regulation going hand in hand up to a point, but beyond that point there is the potential for conflict if the regulation goes too far. I must say, my Lord Chairman, that I have not heard anybody say that the regulation does not go far enough in this area so it is not a concern that we have addressed.

97. It could be, I think, that Brussels might feel that way. There is something that I have heard about lately in this field of regulation which is apparently called the fourth hurdle. Can you tell us something about the other three and rather more about the fourth? What is it?

(*Dr P Baker*) My Lord Chairman, the fourth hurdle is the concept of need for a product which is not a concept that we consider is amenable to regulation. The three primary hurdles for products of any technology, not just biotechnology, are quality, efficacy and safety.

Baroness Platt of Writtle

98. I am sorry, I did not hear what the fourth one was?

(*Dr P Baker*) Quality, efficacy and safety are the three hurdles that all products should meet regardless of the technology from which they are produced. The fourth hurdle is one of need.

Chairman

99. And whose hurdle is it?

(*Dr P Baker*) It is nobody's at the moment, my Lord Chairman, but it is being widely mooted within the Community—

100. You mean the European Community?

(*Dr P Baker*) Yes, the European Community, that the—

Lord Gregson

101. But would that not have strangled the laser at birth?

(*Dr E Baker*) My Lord Chairman, perhaps I may come in here. In the written memorandum we referred to a document which was produced by the European Commission in 1991.

Chairman

102. Can you tell me where that is?

(*Dr E Baker*) I shall be struggling to find the reference so perhaps I may read out the title to the Committee, my Lord Chairman. It is called, "Promoting the competitive environment for the industrial activities based on biotechnology within the Community". That document sets out a broad framework for European Community policy in this area and it was subsequently endorsed by the Council of Ministers. That paper, I think, explains European Community policy towards this fourth hurdle issue. The recommendations include one on the legislative framework that where a biotechnological product is assessed—and we can send this to the Committee later, my Lord Chairman, if that would be helpful—the three traditional criteria based on scientific evaluation apply. By their nature, socioeconomic aspects need to be considered in a different way. It is not the intention to have another systematic assessment in addition to the three criteria. The Commission will normally follow scientific advice. Then it goes on to say that the Commission reserves the right, however, to take a different view in the light of its general obligation to take into account other Community policies or objectives.

103. Let us get back to need. Does not the market determine need?

(*Dr Finer*) I think that that would the view of the Department of Trade and Industry, yes, my Lord Chairman.

104. It would be the view of the Department of Trade and Industry?

(*Dr Finer*) Yes, my Lord Chairman.

105. And would that be the view of Government as a whole?

(*Dr P Baker*) The Food Advisory Committee of the Ministry of Agriculture, Fisheries and Food does consider the concept of need in relation to novel products.

Lord Walton of Detchant

106. My Lord Chairman, there is, however, another possible interpretation in that it might be possible for a government or for the European Commission to say that because this particular process seems so obscure it may not be needed; in other words, they might object to a particular mechanism because they could not see a practical application. That, I think, is a thing that should be resisted because you can never tell in this kind of scientific exploitation what the outcome is going to be until the initial work has been done.

(*Dr Finer*) That is certainly the fear, my Lord Chairman, and we should certainly resist that.

Chairman

107. It all sounds a bit medieval! How do you think the European Community policy on biotechnology is likely to evolve? Presumably you have some input into that evolution?

(*Dr Finer*) My Lord Chairman, the basis for future EC policy on biotechnology is in the communication that Dr Liz Baker referred to with the snappy title, "Promoting the competitive environment for the industrial activities based on biotechnology within the Community", and, as Dr Liz Baker said, that communication was endorsed by the Council of Ministers in 1991. It stressed the importance of biotechnology and set out a framework that covered regulations, standards, protection of intellectual property, research and development and other issues. Flowing from its analysis the Commission suggested a range of actions in particular to solve what they saw as three specific problems, insufficient patent protection, fragmentation of the Community market and the bad image that they say biotechnology sometimes has from both policy makers and the general public. When the Council discussed that it encouraged the implementation of the actions that were proposed by the Commission. That included streamlining testing and authorisation procedures, ensuring that one assessment and notification procedure covers all that is required for product authorisation, which is a very important point, my Lord Chairman, pursuing work on standards, developing and implementing a policy for research and development in biotechnology which is relevant to the future needs of industry and recognising that the protection of biotechnology inventions may need to be improved. They have followed that communication up since by a couple of consultation papers, one of which was a stocktaking, and the other was a comparison of the regulatory framework and research policy on biotechnology within the European Community compared with the United States of America, which has been quite helpful to us. We will be working with our colleagues in other departments, my Lord Chairman, and indeed other Member States and the Commission to ensure that those recommendations are pursued. That therefore is one general area. If I may refer to another area, my Lord Chairman, that is the Community's framework programme number four on research, with which I imagine that you are familiar. As you may know, my Lord Chairman, discussions on this framework programme are still at a relatively early stage, but we have been trying to ensure that the programme focuses on the needs of industry in general and in particular we, the United Kingdom, have led Community wide efforts for a higher profile for biochemical engineering, and that seems to be meeting with some success.

Lord Walton of Detchant

108. My Lord Chairman, may I just say that the written evidence you produced for us I thought was a joy—it was brief, it was succinct and it was very clear, and I enjoyed reading it.

(*Dr Finer*) I am glad to know that, my Lord Chairman.

109. May I take it from what you said that the Office of Science and Technology under Mr William Waldegrave is the lead group in relation to the co-ordination of the programme?

(*Dr Finer*) Yes, my Lord Chairman.

110. If I may just follow up the point about exploitation, to which you referred, it has often been said that in Britain we are very good at inventing and at furthering basic research but not so good at exploiting it commercially.

(*Dr Finer*) Yes.

111. You mentioned about the LINK schemes and the Biotechnology Means Business awareness programme. Is this kind of initiative going to be enough or is it the case that these major committees to which you refer may be in a position to define possible areas very much in need of development in the biotechnology field where perhaps pump priming money from government might have been used to develop these ideas?

(*Dr Finer*) The interface between the research base and industry is perhaps more sharply brought into focus in the are of biotechnology than in many other sciences, that is, the importance of it, and because of that clearly the forthcoming white paper on science and technology that the Government is working on now would be relevant to our area and we have been making an input into that with a view to beefing up mechanisms for transferring knowledge, expertise and sometimes people, of course, at the end of the day, from the science base to industry. Meanwhile we are running out own programmes flat out. Would it be helpful, my Lord Chairman, if I said a little more about the Biotechnology Means Business programme?

Chairman

112. Yes, please?

(*Dr Finer*) It consists basically of a series of seminars up and down the country to which we invite carefully selected firms and we give them presentations by businessmen who have been successful using biotechnology, and while they are there we ask the attendees to fill in a questionnaire to show where there might be opportunities for using biotechnology in their businesses. Over the lunch period we then talk to them and try to draw things out more. The interest is then followed up with visits and advice. We have already been in contact with 500 companies since we started in 1991. We also have a couple of clubs. One is called a diagnostics club, and this was established in 1991 as a forum for the exchange of ideas and to match expertise and requirements on diagnostics. It involves research groups, diagnostic manufacturers and some organisations that promote technology transfer. It is administered by a couple of trade organisations and we are funding that, or rather part of it. There are now 68 organisations who are members and the activities of the club include meetings, monthly news letter, a directorate of members with their expertise and requirements. We have also a water treatment club which was set up last year on a similar basis. These are some of the mechanisms that we are using for that very important issue, my Lord Chairman.

Lord Soulsby of Swaffham Prior

113. My Lord Chairman, may I follow on from what you have just said and partly from what Lord Walton has just said about trying to get small businesses interested in biotechnology. One has the impression, indeed, one is fairly well aware, in respect of the amount of venture capital available for biotechnology in this country despite the fact we can lead in discovering that we cannot translate that into making it at the production level. You say in paragraph 6 that we are "second-order players". Now what is it that will bring more venture capital into this country for biotechnology and then after that the post venture capital to get to the large scale? What are the influences that you can see that allow us not to do as well as, say, the United States, for example?

(*Dr Finer*) My Lord Chairman, it is a very complicated and extremely important subject. We have just allocated a member of my staff to do a lot of work on this. I am afraid that it is very early days yet. The first thing is that we need to investigate just what is fact and what is myth here. I was told last week that it is not as easy to raise venture capital in the USA as some United Kingdom people seeking funds might lead us to believe. Someone from a biotechnology firm in the United States told fairly harrowing stories of how it had taken him really quite a long time to raise the capital that he needed. That having been said there is no doubt that there is a more mature market there for venture capital; it is a bigger market. They are more used to biotechnology than we are here, I think, and I should say that there is more of a risk culture. I do not know whether Liz Baker would like to add anything.

(*Dr E Baker*) My Lord Chairman, I think that Dr Finer has probably covered what I should have said. It is clear that capital availability in general will be a very important determinant of industrial competitiveness and one that is going to become more important as the centre of gravity in this area shifts from the science base into the market. The starting point of any government view on this I think must be to develop a basis of factual evidence rather than anecdotal evidence. As Dr Finer has said, that is one of the tasks that the Department of Trade and Industry has begun.

Chairman] Factual evidence and anecdotal evidence are often very similar.

Lord Gregson

114. What Lord Soulsby mentions is post venture capital. I understand—and I declare an interest in a merchant bank—that the real shortage is post venture capital compared with America. In America it is very easy on the secondary exchange to raise money. We have actually got on in this country now.

(*Dr Finer*) Yes, we have recently been putting some evidence to the Stock Exchange who have issued a consultative document proposing changes to the

[Lord Gregson *contd.*]

listing rules which would permit companies without full history in certain areas to be listed.

115. That was the secondary market, of course, until they stopped it.

(*Dr Finer*) Yes. If that goes ahead, we think that it will be a great help. One of the problems, of course, is: how do you get your money out. If you are a small firm developing a product where it might be even ten years before you get a positive cash flow it may be easy for people to put money in—and perhaps this is just another way of making your Lordship's point—and those people may want to take their money out five years into the game and how do they get it out if there is no positive cash flow?

Chairman

116. You draw attention to the problems of capital investment in paragraph 41?

(*Dr Finer*) Yes, my Lord Chairman.

117. What would you think of the notion of public investment in this field or is that too old fashioned an idea?

(*Dr Finer*) I have not seen any indications, my Lord Chairman, that the Government would look favourably on that sort of thing!

Chairman] From what I read in this morning's papers the civil servants tell the Government what to do!

Lord Gregson] The Secretary of State could intervene before breakfast, of course!

Chairman

118. You do not see that as a likely field of activity, Dr Finer?

(*Dr Finer*) If it turns out that that would be one of the key things to do to enable small companies in biotechnology to succeed, then clearly that would be one of the options that ministers will consider against the background of their general policy.

Lord Whaddon

119. You say that you are not aware of any interest in public investment by our Government. Are you aware of any interest on the part of our partners in the common market, Germany, France and others? Is there any public investment there?

(*Dr Finer*) I am not aware of it, my Lord Chairman.

(*Dr E Baker*) I am not either.

Lord Soulsby of Swaffham Prior

120. My Lord Chairman, there are two points that have been mentioned to me, first of all, from the point of view of potential investors, that being a new technology which few investors understand there could well be a need for some kind of biotechnology audit group that could help investors to understand the technology being proposed to them has actually got some sense in it. Do you see a need for that kind of organisation, either started off by Government or operated as a commercial operation? Then perhaps I could raise the other point that has been mentioned to me, my Lord Chairman, by what you might call biotechnology companies in the soft area of biotechnology rather in the hard area where it is likely to have an impact on what people do in the agricultural field, that is, that they are very hampered by the high cost of testing products that have to go through the same sort of testing procedures as hard technology products might and that is a very costly business for small companies and possibly is not necessary. I wondered whether you might have any comments on that.

(*Dr Finer*) On the first one, my Lord Chairman, I think that it is generally true that if one can somehow give investors confidence that the technology that they might be interested in has some sort of seal of approval from someone it can make a tremendous difference. I have seen this happen in other areas. Sometimes Government can play a role in helping that. For example, I imagine that if a company had gone through the procedures in our Biotechnology Means Business programme—the one that I described before—and had had a visit from an expert we had sent out and the expert had written a report saying, this is a worthwhile project, then the person wishing to carry out the project would have less difficulty in raising funds than had that not been the case. It is also true that at least a couple of the people in this country who act as venture capitalists in this area whom I have met either are themselves experts in biotechnology or they employ experts so that there is not an entire gap between the two.

Lord Flowers

121. In your work on framing regulatory provisions in biotechnology what sort of duty do you have towards industry? Do you have a duty to consult them? If so, how far does the consultation go? Do they really play a part in the regulations that you draw up or do you just listen to what they say and then go away and do what you were going to do anyway, and so on and so forth?

(*Dr Finer*) In some areas departments have a statutory duty to consult industry, but anyway in practice all departments make a point of consulting fully before introducing legislation. On the recent GMO regulations the Department of the Environment and the Health and Safety Executive took the lead in introducing the regulatory framework, of course. Formal consultation was through a committee called the Advisory Committee on Releases to the Environment and another one called the Advisory Committee on Genetic Modification. Both industry and the Department of Trade and Industry sit on those committees. However, there was also extensive informal consultation at specially convened meetings. Once my division was established, which was part way through the consultation process, that brought in an extra dimension because industry had a new focus to which to come, and we are told by industry that many or most of their strongest objections to the early drafts have now been dealt with positively and they are far more happy with the existing legislation than they were with the early drafts. We will continue to consult industry through the Biotechnology Industry Government Regulatory Advisory Group which we mentioned before, which meets at least quarterly and

[Lord Flowers *contd.*]

more often if necessary, specifically to look at the impact of regulation on competitiveness. In addition we have set up regular links with the CBI biotechnology working group and a similar committee in the CIA—Chemical Industries Association, the Association of the British Pharmaceutical Industry and Bio-Industry Association, so we have a great many industry links that we are using to make sure that industry's voice is heard by Government.

122. The other side of the same coin, of course, is: how do you reassure people that you are not in the pockets of industry?

(*Dr Finer*) Yes, that is a very important aspect, my Lord Chairman. Of course, the Department of Trade and Industry itself is not a regulatory department on biotechnology on the whole with some exceptions on the patent side and perhaps where more general issues like company law come into play. Even so, however, it is certainly true that we must not simply act as a mouthpiece, as a parrot, for industry. Among other things we should lose our effectiveness within Government if we were thought not to be applying an intelligent filter because people would quickly stop taking account of what we said, so we do have to apply that intelligent filter.

Chairman

123. On the subject of intellectual property I notice in that paragraph 38 you mention an EC directive but you do not mention the Copyright Act 1988. Is that because the 1988 Act does not apply or is inadequate or what?

(*Dr Finer*) My Lord Chairman, perhaps I may ask Mr Hoptroff to answer that question.

(*Mr Hoptroff*) The 1988 Act was primarily to do with copyright.

124. It includes patents?

(*Mr Hoptroff*) It includes a small amount of amendment to the 1977 Patents Act, which remains the primary instrument governing patent law in this country. Although we talk about intellectual property in this particular context it is really patents that we are concerned with so there is no particular relevance of the 1988 Act to the subject of patents and their relations to biotechnology. The 1977 Act is still the main Act.

125. Why did you not mention it? You mentioned the EC directive only. Why did you not mention the 1977 Act?

(*Mr Hoptroff*) The 1977 Act is a general Act dealing with patents for all subjects. The problem we now have is that patent law generally is trying to adapt itself to this new form of technology. In the past patents applied particularly to mechanical subjects. If there was a mechanial invention and you bought some good embodying that invention from a patentee, and if you then wanted another one you would either have to go back to the patentee and buy another one or you would have to make it yourself, in which case you would clearly be infringing the patent. Because the subject matter of a biotechnological invention may be capable of reproducing itself you have the situation where you may purchase some goods from the patentee which are covered by the patent and which, if you just keep them and feed them, will reproduce themselves so that you will get a never ending supply and never have to go back to the patentee. One of the questions that are having to be addressed is to what extent that self reproduction of patented material is an infringement of the patent.

126. I assume what you mean is that. We have a new tomato which you have all heard about. What would you patent there? Would you patent the tomato or would you patent the process by which the tomato was designed?

(*Mr Hoptroff*) My Lord Chairman, you could patent both. You could have a patent for the process for producing this tomato, which would be incorporating - or perhaps not incorporating, but altering, a gene; and you could also patent the product of that process, which would be the tomato itself. What you would claim in your patent would be any tomato in which a gene had been modified in a certain way so as to prevent its becoming squishy.

127. It is just a little bit like the copyright of a book. A copyright would exist on the intellectual part of the book and there would be a copyright on the book as a printed thing itself. Is that the kind of analogy of which you are thinking?

(*Mr Hoptroff*) My Lord Chairman, I think an analogy between copyright and patent may be rather dangerous because the right of preventing someone copying is not quite the same as preventing someone else producing an article independently.

Lord Perry of Walton

128. Has it been tried yet, if you buy the tomato as a plant or even as a fruit where it is possible to propagate it in your back garden, as to whether, if you do, you are infringing the patent?

(*Mr Hoptroff*) At the moment, my Lord Chairman, I am not aware that this has ever been tested in the courts. The assumption is that it would probably not be an infringement if you just did it in your back garden because it would not be a commercial operation, but if you were to reproduce it commercially and sell those tomatoes then it would be an infringement.

Lord Flowers

129. Perhaps I may return to the question I was asking before. You were kind enough to explain your relationship with industry in carrying out your regulatory process. The regulations that are imposed on industry, of course, affect their competitiveness with each other and perhaps even more important with their corresponding numbers in their countries. How do you try to take into account the competitive position of industry? You can easily impose regulations that could put them completely out of business as far as international trade is concerned. You do not want to do that, so how do you try to balance the various considerations, including competitiveness? Is it your responsibility to do so?

(*Dr Finer*) I think that the Government would see it as a clear responsibility to ensure that its regulatory regime did not put industry at a severe disadvantage compared with other countries. To ensure therefore

[Lord Flowers *contd.*]

that that policy is carried through we do two main things. One is that we keep closely in touch with the industry itself so that industry can inform us where it feels that it is being put at a disadvantage by regulations in this country, and they are certainly not slow. Across the whole field of my responsibilities they are certainly not slow to come to us where that does seem a problem.

Chairman

130. In this respect to what extent do you keep in touch with the commercial counsellors overseas?

(*Dr Finer*) That was going to be my second point, my Lord Chairman. That is the other way that we do it: we do keep in touch with our embassies. We have information, for example, on what is currently felt to be the industry's view of the regimes in the USA and in Japan and in other European Community countries, and if it would be helpful, my Lord Chairman, I could give you a resumé.

Lord Flowers

131. I am particularly concerned at the fact that some countries are sometimes said to change their regulatory regimes in order to improve their competitive position against countries that have not yet changed them. I am just wondering how the whole of that process of international process works.

(*Dr Finer*) My Lord Chairman, the United States of America has issued policy statements that imply that there might be changes in the regulatory regime to improve their international competitiveness. However, as far as we can see the regime as it is presently stands if you look at the detail is not significantly different in most cases from the regime in the European Community.

132. But I thought that the argument about horizontal versus regulation had a great deal to do with the competition?

(*Dr Finer*) Yes, I think that industry is used to having both horizontal and vertical regulation, horizontal regulation on safety and vertical regulation on specific products. The important thing is to make sure that for a specific time consuming thing like a risk assessment they do not have to do it twice, and that is the way that we are trying very hard to ensure that the regulations are applied in this country. Dr Liz Baker may wish to come in here, my Lord Chairman, or indeed Dr Peter Baker.

(*Dr E Baker*) My Lord Chairman, I think that it is fair to add that the regulatory framework, particularly in respect of genetic modification technology, is relatively new and the regulatory framework that governs that both in the European Community and in the United States and Japan is still evolving. Our advice from counsellors at present is that in particular the United States arrangements appear on the face of it more user friendly, but in practice the regulations are probably not significantly less restrictive. I think that this is an area we should be keeping a very close watch on over the coming years and work closely with the departments with regulatory responsibilities.

133. My concern is that if, let us say, the United States gets a head start over us by having a regime that is more user friendly, as you put it, it is very difficult to catch up again because these, after all, are bureaucratic processes changing regulatory frameworks and inevitably they take a long time and a lot of people have to consult and so on. In the meantime you have lost your competitiveness. What I am trying to get at is how you cope with that sort of situation.

(*Dr Finer*) My Lord Chairman, the European Community directives do specifically include the ability to change them in the light of experience. We wil be very carefully monitoring what is going on so that we can try to persuade the Community to make those changes if it seems desirable.

Chairman] I am afraid that we are running out of time.

Lord Perry of Walton

134. Have you considered categorising the regulations in terms of the vastly different products that are involved, some of which will require much tighter regulation than others?

(*Dr Finer*) My Lord Chairman, I think that that really has to be a question for the regulatory department.

135. You have not had pressure from industry to do just that?

(*Dr P Baker*) As the technology is developing, my Lord Chairman, directives in specific product areas or product sectors are gradually coming forward. As experience with the technology develops then there will be a greater movement towards what might be termed vertical or product oriented legislation. If I may just quote an example here, my Lord Chairman, there is a draft regulation on novel foods coming forward and in that regulation the environmental risk assessment for the novel food is equivalent to the environmental risk assessment under the deliberate release directive, thus avoiding what I believe industry is most concerned about, that is, dual regulation, namely, two hurdles for the same thing, for the same product. It is essential and one of the key efforts of this department is to make sure that there is not dual regulation of products, whether it is food, pharmaceuticals or whatever.

Lord Walton of Detchant

136. I do not want to bowl you a googly at the end of your evidence, but I should like to ask whether you have any comments on the ethical issues that arise over patenting in the field of human health. For example, there have been suggestions recently that certain products used for gene therapy which are beginning to emerge might be patented in the United States and there was a recent storm about a proposal by a scientist to patent a technique of cell transfer therapy. What would be your views about this?

(*Dr Finer*) My Lord Chairman, I do not think that the Department of Trade and Industry has any views on the ethical problems, or supposed problems. They are being handled by the Ministry of Agriculture, Fisheries and Food and the Department of Health.

Lord Walton of Detchant] I just wanted to clarify your position on that, thank you.

Chairman

137. We must draw to a halt there, Dr Finer. If there are any additional or further explanations that you wish to let us have I hope that you will feel able to do so. We should also like you to let us have a brief note on the relations that you have with the overseas commercial counsellors.

(*Dr Finer*) Certainly, my Lord Chairman.

Chairman] Thank you very much.

Supplementary evidence from the Department of Trade and Industry

Controls over Genetically Modified Organisms (GMOS) in Japan

1. The Japanese government prefers guidance to regulation in controlling GMOs. Five government bodies issue such guidance. So far, over 30,000 rDNA experiments have been carried out without incident. By March 1992 there were 195 industrial-scale processes based on rDNA technology. An organisation wishing to carry out experimental or industrial research needs to address the appropriate government body.

—the *Ministry of Education* (MOE) for research in national and private universities;

—the *Science and Technology Agency* (STA = OST equivalent) for laboratory scale (< 20 litres) research in national and private sector institutes;

—the *Ministry of Agriculture, Fisheries and Forestry* (MAFF), the *Ministry of Health and Welfare* (MHW) or the *Ministry of International Trade and Industry* (MITI) for industrial applications. (For example, the MHW is responsible for pharmaceutical use and the MAFF for farm use.)

2. Each body has issued detailed guidelines which are updated in the light of experience. Translations are available in English. The MOE and STA guidelines at least are closely modelled on the US National Institute of Health. They set out basic conditions for rDNA experiments and also cover management responsibilities and procedures, storage, transport, training and health. Non-standard experiments using microbes or cultures cells as hosts require prior approval. Routine experiments do not.

3. In practice, a research programme can easily fall into the jurisdiction of more than one body. Industry has called for the consolidation of the different sets of guidelines. But no change is likely in the near future. A White Paper produced by the Environmental Agency in 1991 argued for a move from guidance to regulation, implying the rDNA technology could be environmentally damaging or even dangerous. It has been shelved following intense lobbying from the Ministries involved.

4. Guidelines issued by MAFF, MHW and MITI on controlled large-scale industrial use and deliberate release of GMOs follow OECD guidelines, which the Japanese government helped draft. A MAFF-supervised safety evaluation is required before GMOs can be released into the environment. There have so far been no commercial attempts to do so, though MAFF have completed the final stage of testing, in open fields, of a recombinant tomato.

Control over Genetically Modified Organisms (GMOs) in the USA

DELIBERATE RELEASE

1. Three agencies have responsibility for regulatory control of agricultural biotechnology in the United States. These are the United States Department of Agriculture's Animal Plant and Health Inspection Service and Food Safety and Inspection Service, the United States Environmental Protection Agency, and the Department of Health and Human Services' Food and Drug Administration. The regulatory requirements are broad in scope and intended to protect the public health and environment, promote free trade, and ensure that products in the market place are safe and effective for their intended uses and are truthfully labelled. Risk is examined on a case by case basis but as safety information accumulates it is intended that ultimately releases will be placed in categories of increasing risk and handled accordingly.

2. Permits are required for release into the environment (use outside constraints of the physical confinement of a laboratory, contained greenhouse or fermentor) of a regulated article (any organism that has been altered or produced through genetic engineering if the donor organism, recipient organism, or vector is included on a designated list of genus or taxon, or is of unknown classification). Permits are also required for introduction and field testing of transgenic animals and fish.

3. Both the United States Department of Agriculture and the Food and Drug Administration have recently published proposals to make modifications to their regulations, but these are still subject to general debate.

4. Individual States, counties, and towns are at liberty to modify federal regulations relating to environmental release of GMOs and in some circumstances do. Such regulations are generally more restrictive than federal regulations and are too variable to be summarised here.

CONTROLLED USE

5. Agencies of the Department of Health and Human Services have established recommendations for the safe use of infectious agents. In particular the Centers for Disease Control and the National Institutes of Health set out standard and special microbiological practices, safety equipment and facilities which are recommended for working with a variety of infectious agents, including GMs, in research in laboratories in both academia and industry.

6. The National Institutes of Health has published guidelines for the contained use of DNA organisms which recommend physical containment at specific levels for different experiments and exempt other experiments from containment requirements. The appropriate large-scale containment requirements for many low-risk DNA derived industrial micro-organism is no greater than those appropriate for the unmodified parental organisms. The NIH guidelines are not a legal requirement but are enforced on all researches using GMOs who receive any kind of federal grant.

7. In this case also States are able to enforce additional regulations if they so desire. For instance the State of California regulates the movement of organisms within the State. They require special permits and inspection of the receiving laboratory. Since any laboratory working with GMOs would have to receive at least some materials from outside it would therefore be subject to a safety inspection.

COMMENT

8. There are a multiplicity of federal agencies, State and other jurisdictions involved in the regulation of GMOs in the United States. This has led to a degree of overlap and conflicting regulations. The extent to which control is "risk-based" in some circumstances and "process-based" in others, depends on the views of the particular agency enforcing the regulation. In 1990 the President's Council on Competitiveness suggested that "... regulations and guidelines affecting biotechnology [should be] based solely on the potential risks and [should be] carefully constructed and monitored to avoid excessive restrictions that curtain the benefits of biotechnology to society". These recommendations have not yet been introduced into regulatory control of GNOs but may be in the future.

Written Evidence from the Ministry of Agriculture, Fisheries and Food (MAFF)

EXECUTIVE SUMMARY

1. MAFF has interests in traditional biotechnologies as well as novel ones, in particular genetic modification on which this paper concentrates. These interests are based on its responsibilities as a regulator and its aim of improving the economic performance of the agriculture, fishing and food industries.

2. MAFF's regulatory functions cover a wide field: from more general responsibilities for animal and plant health matters, farm animal welfare and food safety and labelling, to the assessment of specific ranges of products, namely:

Veterinary medicines

Agricultural pesticides

Crop varieties

Animal feedingstuffs and their additives

Novel foods

Food additives

Agricultural fertilisers.

All of these products can consist of or contain genetically modified organisms (GMOs) or can be produced through the use of genetic modification (GM) technology.

3. GM technology appear to hold great potential in MAFF's area of responsibility. Examples are given to illustrate the range of possibilities.

4. MAFF considers that regulation has to strike a balance between imposing constraints on industry and assuring the public about the safety of genetically modified products. Over-regulation needs to be avoided.

5. Regulation is however only one of the issues affecting the successful commercial application of GM technology. Public and consumer attitudes are also important. These will be influenced in part by the establishment of an appropriate and effective regulatory system. But it is also necessary to ensure that the public is better informed about the science of genetic modification and that arrangements are made to address some of the broader ethical issues. Industry has a specific role in promoting the use of GM technology and its products.

MEMORANDUM

A. MAFF'S INTERESTS IN BIOTECHNOLOGY

Q1. What is your interest in biotechnology?

1. The term "Biotechnology" has acquired a range of meanings, from that defined in the "Spinks" Report★—"the application of biological organisms, systems or processes to manufacturing and service industries"—to a synonym for genetic modification (GM) technology. This paper concentrates on the latter. Other novel biotechnologies will also be mentioned where relevent, but MAFF has assumed that traditional biotechnologies such as brewing, breadmaking and cheesemaking are outside the scope of the Sub-Committee's inquiry.

2. MAFF has interests in genetic modification through its responsibilities as a regulator and through its aim of improving the economic performance of the agriculture, fishing and food industries. Its regulatory functions cover a wide field: from the assessment of specific ranges of products to more general responsibilities for animal (including fish) and plant health matters and for food safety, food labelling and farm animal welfare.

3. The specific products for which MAFF has regulatory responsibility (exercised jointly with other Departments) are:

Veterinary medicines
Agricultural pesticides
Crop varieties
Animal feedingstuffs and their additives
Novel foods
Food additives
Agricultural fertilisers.

4. All of these products can consist of or contain genetically modified organisms (GMOs) or can be produced through the use of GM technology. As GMOs, these products are at present subject to the "horizontal" legislation set out in the Genetically Modified Organisms (Contained Use) Regulations 1992 (SI No. 3217) and Genetically Modified Organisms (Deliberate Release) Regulations 1992 (SI No. 3280), as amended (SI 1993 No. 15) relating respectively to the contained use of GMOs and their deliberate release, both at the experimental and marketing stages. The Health and Safety Executive (HSE) and the Department of the Environment (DOE) respectively take the lead on these Regulations. But the *products* are also subject to the existing "vertical" product legislation. This normally extends beyond the protection of human, and where relevant animal, health and the environment and includes requirements relating to quality, efficacy and consumer protection (ie labelling).

B. IMPORTANCE OF BIOTECHNOLOGIES

Q2. How and why is biotechnology important to UK industry?

Q3. What future prospects and opportunities does the technology offer?

5. MAFF shares the view expressed in the Report of the Advisory Council on Science and Technology "Developments in Biotechnology" (1990, ISBN No. 0 11 430045 3) that the new plant and animal biotechnologies "are now showing great potential" (paragraph 3.2). A few examples may help to demonstrate both the scale and the breadth of opportunity.

6. In the field of veterinary medicines, GM technology has to date largely been used to provide alternative methods of undertaking existing processes. For example, it has long been known that certain proteins could have uses in veterinary medicines, but traditional means of obtaining them have been prohibitively expensive. The discovery of ways to programme protein-producing bacteria safely to produce commercially viable quantities of chosen proteins has already led to the development of a range of products, including licensed vaccines against leukemia virus in cats and *E. coli* infections in pigs, and somatotropins which some companies are developing with a view to obtaining licences for their use as yield enhancers in livestock husbandry. Gene-deletion techniques, which replicate mutations which occur spontaneaously but at random in nature, have speeded up the development of gene-deleted vaccines, sometimes with an increased safety factor. Examples are a range of vaccines against Aujeszky's disease in pigs.

7. Future opportunities include the great potential for the development of new types of product. One example, work on which is still at an early stage, is designed to overcome the problem that Newcastle and Gumboro disease vaccines, for use in poultry, are derived from the naturally occurring pathogenic viruses.

★"*Biotechnology*" the Report of a Joint Working Party of the Advisory Council for Applied Research and Developnment and the Advisory Board for the Research Council's 1980, ISBN No. 011 630 816 8.

The vaccines have the disadvantage that these viruses tend to self-regenerate with the risk that they may revert to their natural virulence, thereby spreading rather than controlling the disease. Biotechnological developments have opened up the possibility that the antigens (immunity producing elements) of these viruses could be incorporated into a different, mild poultry virus, and so confer protection from these diseases with much lower risks.

8. The use of GM technology is also of major importance in plant breeding. Successful plant breeding depends on exploiting the available genetic variability in order to create new genetic combinations from which new varieties may be selected. Traditionally, the methods used have been based on hybridisation between breeding lines and varieties of the same species. More sophisticated techniques have already been developed to deal with more distantly related species. These include, for example, the addition of chromosomes by manipulative techniques using aneuploids of the crop plant as the parent. Other indirect systems of creating genetic variability include induced mutagenisis by techniques, such as nuclear irradiation and colchicine treatment, and somatic cell hybridisation by protoplast fusion. Genetic modification techniques, in which gene transfer from either a related or unrelated species or even from non-plant species, achieved by the use of biological vectors, electroporation, microinjection or ballistic techniques, may be seen as the most sophisticated systems of creating useful genetic variation.

9. The advantage of the new genetic modification techniques is that they are designed to introduce directly a specific trait into a known genetic background. With the other techniques a large amount of additional genetic material is introduced along with the desired trait. However, even though specific traits may be introduced using gene transfer, it is not possible always to predict the behaviour of the transferred gene in a given genetic background. As a consequence, it is necessary to conduct field tests, to confirm that the new variety has the desired characteristic, in the same way as for lines developed by conventional techniques. Therefore gene transfer may be considered as part of a continuum of techniques to create new combinations of genes from which improved plant varieties may be developed.

10. The use of GM technology means that desirable traits which were previously unavailable in a species can now be introduced. This has the potential to allow plant breeders to develop varities with high levels of resistance to pests and diseases so that crops can be produced with reduced use of pesticides.

11. There are environmental benefits to be gained from this, as well as benefits to the farmer and consumer through reduced costs of production and less exposure to potentially harmful chemicals. To date, potato and tomato have received the most attention in relation to pest, disease and virus resistance. Product quality may also be improved by gene transfer. This may be for example through the reduction of naturally occurring toxins; through increasing the proportions of the most disirable components in edible oils; or increasing the starch to sugar ratio in the tubers of potatoes.

12. In some cases the objective of a genetic modification programme will be to improve the nutritional or food quality characteristics of crop varieties. For instance, the "Flavr Savr" tomato developed in the USA by the American company Calgene Inc. and an equivalent development by Zeneca Seeds (formerly ICI Seeds), are designed to improve product quality—ie their keeping and processing characteristics. The first products in this sector are close to market and further commercial developments are likely within the next five years.

13. The use of gene transfer techniques in plant breeding is at an early stage of development. A rapid rate of increase in the introduction of new varieties resulting from the introduction of these techniques has not yet been realised. This is partly because the technology is difficult and expensive, and new varieties resulting from these techniques require almost as long a development period as varieties produced by conventional methods. To date no genetically modified varieties of agricultural crops have been released for marketing in EC. During the period 1986–92 a total of about 1,000 approvals to conduct field trials on genetically modified varieties have been granted in Europe, North America, Australia and Japan (unpublished OECD data). Some 65 of these have been carried out in the UK.

14. The range of biotechnology applications to food is wide. Many employing more "Traditional" biotechnologies are already in commercial operation such as the bioconversion (enzymic modification) of vegetable oils and the production of amino acids and other specialised nutrients by fermentation. The first food ingredient produced by genetic modification—a bakers yeast—was cleared for use by the Advisory Committee on Novel Foods and Processes in 1991 although it has yet to be used commercially. Further genetically modified baking and brewing yeasts, and modified food bacteria to impart improved flavour or quality, are feasible and likely to come into commercial operation within the next 5–10 years. Genetically modified microorganisms also have potential applications as feed additives, most importantly as "probiotics" which enhance the digestibility of feed.

15. A number of food additives and processing aids, including enzyme preparations, are produced by traditional fermentation technologies using microorganisms. Genetically modifying these microorganisms can lead to more efficient and economic production of additives and processing aids. In the case of enzyme preparations an additional benefit is that those derived from genetically modified microorganisms are generally purer than those produced by means of more conventional technology.

16. The use of genetic modification in animals for food purposes is likely to be longer term. This reflects in part greater technical difficulties involved. But research interest may well be less, owing to the greater perceived problems of consumer acceptance.

C. SAFETY AND REGULATION

Q4. *Which developments in biotechnology raise issues of safety and how should they be addressed?*

Q5. Should biotechnology by regulated by an industry specific regime?

Q6. From a technical point of view, is horizontal regulation (where a product is judged through the process by which it is derived) better than vertical regulation (where a product is judged by its characteristics)?

Q7. Should regulation evolve from a horizontal to a vertical approach in each industrial or environmental application?

Q8. How do current regulations compare with those of other competitor countries

—In Europe

—in the Far East

—the USA?

17. All new developments and technololgies carry risks, as do existing technologies and process systems. Products such as medicines and pesticides, for example, are potentially hazardous which is why they are strictly regulated. Regulation is based on scientific assessments designed to ensure that the risks to people, animals and the environment are contained well within acceptable limits

18. Products are therefore usually regulated because of the risks that they present. However, the public perception of the risks may influence the decision on whether or not to regulate. This was a factor in the decision, taken at European Community level, to introduce specific controls on GMOs. A further factor was the risk that, in the absence of a harmonised Community regime applying to GMOs, individual Member States would introduce their own rules. This would have seriously impeded the establishment of a single market in GMOs and their products.

19. This process-based or "horizontal" approach to regulation has the advantage that it is all-embracing. It improves the likelihood that foreseeable calamities, which arise from the nature of the technologies and could persuade the general public that a technology as a whole was unreliable and unsafe, can be prevented by regulation. This carries a special force for research where the results of a particular procedure are necessarily harder to predict.

20. But there is a negative side to "horizontal" regulation, particularly at the marketing stage. The need to provide safeguards which are able to take account of the most hazardous products means that a single regulatory system inevitably bears unnecessarily on those products which are unlikely to present significant hazards to the public and to the environment. The risks from vaccines, for example, are arguably much greater than from a novel plant variety which is unlikely to survive outside the cultivated environment. A single approach to risk assessment, based on a standard set of questions, can therefore present problems for particular product sectors.

21. Process-based regulation is moreover insufficient. This is in fact recognised by Directive 90/220 which envisages in Article 10.1 that a consent to place a product on the market may need to be complemented by the requirements of relevant product legislation. It also provides in Article 10.2 for EC product legislation to take over the approval task entirely once it has been adapted to provide similar safeguards to the Directive.

22. As well as the scope for derogations to appropriate product legislation, Directive 90/220 has provisions for simplifying applications for deliberate release consents and for amending the technical requirements of Annexes II and III by regulatory committee procedure (see Article 21). As more experience of deliberate releases is gained these provisions offer the means to adapt the Directive's requirements to the degree of risk and uncertainty involved in any particular class of proposal.

23. A further benefit of "vertical", ie product, legislation is that it means that all products of one type of commodity are subject to the same standards of safety no matter what technology was involved in making them. Having separate regulatory approaches to the marketing of products would inevitably mean that there was a risk that different safety standards would apply to similar products, simply on account of the process by which they were made.

D. INDUSTRY CONCERNS

Q9. *What are the consequences, or likely consequences, of the regulatory regime on competitiveness of the UK industry, in particular as regards*

(1) research

(2) product development

(3) investment

(4) location

(5) sales and marketing?

Q10. *Is there a danger that the present regulatory regime will prevent the exploitation by British industry of research conducted in the UK science base?*

Q11. *How best can issues of public acceptance be addressed?*

Q12. What other factors do you consider will play a crucial role in the competitiveness of the UK biotechnology industry?

24. The EC Deliberate Release Directive provides a statutory basis to reassure the public throughout Europe that the products of GM technology can be used safely. Harmonisation of EC law in this area also establishes a level playing field in which industry can operate.

25. Regulation must however strike a balance between imposing constraints on industry and providing reassurance to the public about the safety of products of GM technology. Over-regulation would adversely affect UK and EC competitiveness. At the national level we must ensure that in implementing Community rules the UK does not impose greater burdens than those provided for by the EC Directive. It is particularly important that the exploitation of the UK's strong research base in GM technology (as noted in the ACOST report) should not be hindered by inappropriate regulation.

26. Regulation is not the only factor which impacts upon the successful commercial exploitation of GM technology. Other obstacles have also to be addressed. The principal one is whether the products of GM technology will be accepted by consumers.

27. There is likely to be a particular problem in this area with foods which are either sourced from GMOs or have been processed using GMOs especially where the foods may have been sourced from genetically modified animals. Many consumer groups have urged that all foods sourced from or using GMOs should be labelled specifically to identify them as, in some sense, products of genetic modification. Some have even urged that such foods should be boycotted. The reasons for such views are at present unclear, although a lack of information about or awareness of what is being done, or proposed, may contribute to demands for labelling. Industry interests are generally opposed to a specific labelling requirement. Amongst their reasons are concerns about practicality and costs, as well as fears that a generic labelling requirement would adversely affect consumer attitudes.

28. The Food Advisory Committee (FAC), which advises Ministers on food labelling questions (amongst other matters), has been reconsidering its guidelines on the labelling of GMO foods and is about to issue a further consultation paper on this subject. The paper will be made available to the Select Committee as soon as it is issued.

29. Consumer and broader public concerns can be addressed by making more information available to the public, and to consumers in particular, about genetic modification. To this end, MAFF has produced three 'factsheets' in the 'Foodsense' series which aim to set out accurately but in a relatively simple way what genetic modification is, how it is regulated, and why it is important. Copies are enclosed for the Sub-Committee's information. However, these can only deal with the issues in a general way. More specific concerns about individual products or proposals can effectively be met only by information from the companies or research organisations directly concerned.

30. Ethical concerns have also been expressed about the potential application of genetic modification to food production. It is difficult to see how these can adequately be addressed through the regulatory process, which is designed essentially to protect humans and the environment. It was for this reason that the Minister of Agriculture, Fisheries and Food and the Secretary of State for Health established, in September 1992, a study group under the Chairmanship of the Reverend Dr John Polkinghorne, President of Queens' College, Cambridge, to look at these broader ethical concerns. The Group is looking specifically at dietary concerns such as those arising from the transfer of animal genes to plants and the implications for vegetarians. The Group aims to present its report to Ministers this summer.

31. In conclusion, MAFF sees the role of Government in providing a regulatory system for GM technology which balances the burdens on industry with the need to reassure the public while providing effective safety controls. Government also has a role in sponsoring appropriate research (not addressed in this paper), and in ensuring that sufficient factual, unbiased information is available to the public about GM technology and their implications. But it is for industry itself to promote these technologies as such and to ensure their acceptance, and that of their products, in the market-place.

19 March 1993.

Examination of witnesses

MR P MURPHY, Pesticides, Veterinary Medicines, Emergencies and Biotechnology Group, and MR J BAINTON, Head of Biotechnology Unit, Ministry of Agriculture, Fisheries and Food, called in and examined.

Chairman

138. Thank you very much for coming, Mr Murphy and Mr Bainton. Would you please tell us who you are and perhaps give us a little bit of background on the Ministry of Agriculture, Fisheries and Food?

(*Mr Murphy*) Thank you, my Lord Chairman. I am Pat Murphy and I am head of pesticides, veterinary medicines, emergencies and biotechnology group, and the responsibility rests with me to co-ordinate my Department's interests in biotechnology. I have with me John Bainton, who is the head of the Biotechnology Unit within the department. The unit has a co-ordinating responsibility for the departmental interest in biotechnology, particularly the regulation thereof. Perhaps I should make one or two comments just to highlight one or two points in the memorandum, my Lord Chairman, which might be helpful. First of all, I should like to draw attention to the importance of biotechnology, and specifically in genetic modification, for the agriculture and food industries. It is important because of the power of the technology, in particular, the capacity to achieve quickly what could only be achieved over many years or even centuries by more conventional technology. Also because of its range, it has applications in virtually all sectors of agriculture and food production. And because of its innovatory capacity; its ability to do things that simply cannot be done by using other technologies. Some examples of the kind of developments that are likely to be commercially viable in the relatively short term are provided in the memorandum and in the Fact Sheets. However, I am sure that these will be enlarged upon by others who give evidence, particularly from industry. Secondly, perhaps I may say a brief word about the department's regulatory responsibilities. We take the lead in the regulation of specific products for marketing, pesticides, veterinary medicines, novel foods and most crop varieties and feedingstuffs. The Health and Safety Executive and the Department of the Environment take the lead on the horizontal legislation relating to genetically modified organisms and the contained use and deliberate release regulations, but the latter are administered jointly with the Minister of Agriculture, Fisheries and Food where his specific responsibilities are concerned. The horizontal regulations reflect the requirements of the relevant Community directives. There is therefore a harmonised Community system. The product or vertical regimes are also harmonised or are in the process of being harmonised at Community level and it is significant that as part of this process some of the key requirements of the horizontal rules are being incorporated into the product legislation. The Council of Ministers has already agreed on such provisions for medicines, both human and veterinary, which in effect would disapply the marketing provisions of the deliberate release directive at the stage where genetically modified organism medicines are put on the market. A similar proposal is before the Council in relation to novel foods, as representatives of the Department of Trade and Industry mentioned earlier, my Lord Chairman. One is expected shortly on pesticides and one on animal feedingstuffs. The Government fully supports the poilcy of replacing horizontal rules by product specific rules at the earliest opportunity, and I can enlarge on this if the Committee wish, my Lord Chairman. Finally, in addition to its regulatory responsibilities the Ministry of Agriculture, Fisheries and Food has as one of its published aims that of improving the economic performance of the agriculture, fisheries and food industries. In view of the importance of genetic modification technology for the future economic performance of these industries there is a clear need in the view of the Ministry of Agriculture, Fisheries and Food to ensure that the way the technology is regulated is appropriate, that is, that it achieves the right balance between providing reassurance to the public about safety of modified products and allowing those applying the technology to become or remain competitive. It is the department's aim to achieve such a balance so far as it is practicable to do so.

139. Thank you very much, Mr Murphy. As I read your evidence and from what you have said you favour moving towards vertical rather than horizontal regulations?

(*Mr Murphy*) That is true, my Lord Chairman, particularly where ther are existing product regimes. If you take pesticides it makes no sense, for example, to have a risk assessment procedure that covers human and environmental safety for the generality of pesticides and which a GMO pesticide would need to go through anyway before it was allowed to be marketed and to have separate from that a further risk assessment under horizontal legislation. So it makes a lot of sense in those cases to move to product legislation, vertical legislation, at the earliest opportunity, and that is certainly the aim.

[Chairman *contd.*]

140. Is there any scientific basis for this preference or is it purely one of industrial convenience?

(*Mr Murphy*) I suppose that it is really a practical argument, my Lord Chairman, in that if you are talking about a GMO based pesticide what you are looking at essentially is its use as a pesticide. Those who are experienced in the use of pesticides are probably best able to carry out that risk assessment rather than experts who have a broader remit and who are looking at genetically modified organisms in their generality. It is easier also for the industry who are involved in manufacturing pesticides to relate to a particular group of experts whose responsibility is the risk assessment of pesticides, both the human safety aspects and environmental safety.

141. If my memory is correct—which it might not be—I seem to recall that the Department of the Environment evidence was less clearly directed towards vertical than horizontal. Is there any difference of opinion between you and the Department of the Environment?

(*Mr Murphy*) I do not think so, my Lord Chairman. My remarks were addressed to those areas in particular where there is existing product legislation. There are areas where there is no specific product legislation dealing with the human or environmental safety of genetically modified organisms. As an example, I think of certain plant varieties though I suppose that you could say all plant varieties really—where the product regime relates essentially to quality matters, that is, marketable quality matters—are the varieties distinct, uniform and stable and are they of satisfactory value for cultivation and use. There is not a specific human or environmental safety assessment built into that procedure. I think that you can say the same also for novel animals, varieties or breeds of animals, where there is no vertical product regime assessing new breeds of animals as such. Therefore, if you did not have horizontal rules in those areas there would be no human or environmental safety assessment at all. It is a question of whether you actually need that. The fact is that it is there at Community level and in the horizontal rules and we have to apply those. My remarks were essentially addressed to those areas where you have specific product legislation and the need to avoid duplicating the risk assessment.

142. So the European Community looms very large in this whole field, does it not?

(*Mr Murphy*) It is virtually entirely harmonised, my Lord Chairman.

Lord Perry of Walton

143. Are the GMO pesticides that you are referring to viable or are they not viable or are they both?

(*Mr Murphy*) If they are not viable they are not GMOs, my Lord Chairman.

144. They could be produced by GMOs?

(*Mr Murphy*) They could be produced by genetic modification technology, but they might not be actually organisms at the stage they are marketed.

145. But at the moment they are all viable, that is, the ones that you are talking about?

(*Mr Murphy*) There are not any GMO pesticides on the market at present.

Lord Wade of Chorlton

146. If I may come in here, my Lord Chairman, from what you have said and from what you have written you believe very strongly that this is a great opportunity for British industry to develop products in the agricultural field and you refer to the regulations that are now unified throughout Europe, but it is one thing having uniformity of regulation and it is another thing having uniformity of enforcement, and it is the enforcement of the regulations that can create very much of a different attitude to what is allowed and what is not allowed. As much as you look closely at the regulations, do you make sure that enforcement is not different and that again our industry might be at a disadvantage because we might enforce the regulations in a different way from somebody else?

(*Mr Murphy*) If I may, my Lord Chairman, I will ask Mr Bainton to answer that.

(*Mr Bainton*) My Lord Chairman, the horizontal regulations are enforced in this country by the Health and Safety Executive who are one of the two joint competent authorities. The Ministry of Agriculture, Fisheries and Food is not directly involved in enforcing these horizontal regulations at all. I understand from the competent authorities that they have a continuing programme of ensuring that the dangers you have suggested do not arise and there is an exchange of information about methods of enforcement and standards of enforcement and this is kept under continual review. It is not something that this department is directly involved in because we do not enforce the horizontal regulations.

147. If I may just follow up on this, my Lord Chairman, you do say in the beginning that you consider improving economic performance of the agricultural, fisheries and food industries is part of your responsibility so you cannot really ensure that that responsibility is being carried out and our industry does have these full opportunities unless you are aware that we are not being differently treated from our competitors?

(*Mr Bainton*) I should agree with you that we need to be aware, but we are not directly involved.

148. Do you not think that you should be? That is the point that I am making.

(*Mr Bainton*) It has been represented to government departments as we set up the horizontal regulations that industry was very anxious that there should be a single enforcement body and that there should not be multiple inspectors coming round looking at various interests so I think that it is a matter of finding the simplest and most straightforward way of doing these things, to have one enforcement body in Great Britain and the interested departments liaising closely with it, so we get information, if you like, second hand, but it is pretty good information from the Health and Safety Executive and the Department of the Environment.

(*Mr Murphy*) My Lord Chairman, if I may come in here, I think that we should be concerned, clearly, if there were major differences in the way the

[Lord Wade of Chorlton *contd.*]

regulations are implemented in different Member States and that would be a matter of concern for us. I am sure that we should wish to reflect that in the appropriate quarter.

Lord Whaddon

149. You will be aware, Mr Murphy, that in eastern Europe there have been a number of environmental disasters. The method there at the moment is, get in and do anything if it will make a few dollars. There is also quite a substantial science base and they are also very big food producers. They are also applicant members of the common market. Are you in touch with those governments to ensure the development of proper regulatory regimes there?

(*Mr Murphy*) In terms of trade, my Lord Chairman, if those countries wish to trade in agricultural products with the Community then their exports would have to meet the standards that are laid down in Community rules.

150. Cross border infections and disasters do not necessarily wait for trade?

(*Mr Murphy*) If there were problems of the kind your Lordship mentions, if there were a threat, we should certainly be in touch with the countries concerned.

151. You are not in touch now to try to stop these disasters happening?

(*Mr Bainton*) The Community at the present time cannot impose its will on third party countries except when they are exporting GMOs to us. Any GMOs exported to any Member State of the European Communities would have to meet the requirement of directive 90/220 as it would be a traded product. As far as what they are doing in their own countries is concerned the OECD has set up the group of national experts on the safety of biotechnology and that is a way by which if you like we can advise them, and Ministry of Agriculture, Fisheries and Food takes part especially on the food safety side. Environmental considerations that seem to be close to what you were suggesting are, of course, for the Department of the Environment to lead on, but the British Government is strongly involved in the OECD discussions on the safety of biotechnology.

Lord Soulsby of Swaffham Prior

152. My Lord Chairman, perhaps I may turn to the industry concerns. On the question of the small businessman or small producers you heard previously from the Department of Trade and Industry of their Biotechnology means Business and probaby in the field of agriculture there is more opportunity for the small business to get into this field than any other industry. One of the concerns is that the regulation and the ultimate registration of the product may lead to constricting in terms of time to the small person who wants to get into it. Do you have any thoughts on that, how that might be alleviated and how the small individual or the small company might want to go along these lines without the constraints—although they might be only apparent constraints—of time, regulation, finance and ultimate registration?

(*Mr Murphy*) My Lord Chairman, it is important that the regulatory system is no more onerous than it has to be to achieve its objective. As a department we keep in close touch with the industry associations representing the type of companies who will be involved in the production of products that will be marketed in the agriculture and food sectors, for instance, plant breeding and the veterinary medicines industry and so on. We are very conscious of the need not to over-regulate and to be responsive to their particular needs. If they make specific representations to us or we learn of a particular problem then we attempt to take note of it in the product regulations and in discussions with the other departments concerned to give effect to their concerns there.

Baroness Platt of Writtle

153. Several times today people have emphasised the importance of a pivot between public acceptance and the need for the credibility of the regulation system, which is clearly vital to the whole thing. I was looking at your food sense Fact Sheet, which seemed very interesting and good at putting it over in a simple way. How does the public get hold of this? Do they go into doctors' surgeries, do they go into schools, do they stand around in supermarkets? How would any member of the public get a chance to read one of those?

(*Mr Murphy*) Thank you for the comments about the Fact Sheets. They are available on demand at the moment. We are proposing to produce shortly a more simplified version incorporating all three fact sheets which will be produced at what we call a higher level, that is, it will be more readily available than these. We have not in fact taken the step of being proactive in their distribution, but that is something that we are prepared to consider, if there is a clear demand for them. Perhaps I can ask Mr Bainton to communicate what we demand we have had so far.

(*Mr Bainton*) My Lord Chairman, I believe that we have issued about 2,000 sets so far, that is in about 12 months. The Food Sense series has four levels of information. Level one is a very glossy booklet on the whole range of the ministry's regulations of food and food safety. That has an index and it refers to other leaflets in the series. The Fact Sheets do not stand alone but they are referred to in other documents. When people approach the ministry for information this is one way that we can assist them. That is the way that they have been distributed so far.

Chairman

154. It seems fairly low key operation, yet is it not important if this sort of biotechnology is to be promoted because there must be a good deal of public information very readily available, especially in relation to food?

(*Mr Bainton*) If you will allow me, my Lord Chairman, there is a question of whether the information is available and whether we are in fact trying to disseminate it at a very high propagandist level. We are trying to explore the right level. We have been criticised by some lobbies even for this very small first step, in that perhaps we are not being quite

[Chairman *contd.*]

balanced, so there is a question of balance given our regulatory responsibilities to observe. If the Committee took the view that we are being too timid I am sure that we should consider that very carefully in future.

Baroness Platt of Writtle

155. My Lord Chairman, I think that this is very important. I belong to the committee on public understanding of science and we are particularly anxious that there is not the science base among the general public. I should have thought that women's organisations are a very important area such as, if we start at the top, the WI, Townswomen's Guild or something like that, and they would then disseminate among their members and in their journal—not necessarily all your leaflets. The other thing particularly is the primary schools where they are doing so much work on environmental protection, which may be biased in the other way. One wants to get both sides of the question explored, I should have thought.

(*Mr Murphy*) My Lord Chairman, this is something that we are giving a lot of thought to. We are still feeling our way. This was our first attempt at issuing any what you might call government information to the public on genetic modification technology. I do not think that other departments have even gone this far. What we were conscious of not wanting to do was to create the wrong impression that we were, as Mr Bainton said, pursuing a propagandist role. However, I think that we are ready to consider a higher profile activity if we can be reasonably certain of doing it without provoking an adverse reaction.

Lord Wade of Chorlton

156. My Lord Chairman, perhaps I may just comment on that. It seems to me rather odd if you are saying on the one hand you have a regulatory aspect and therefore through that you are going to have influence on the industry and how it develops. I should have thought it follows that you have equal responsibility to make sure that everybody knows the true facts of the case. If you were to say, the market is a free market, then of course you are not involved in it at all, but Government and people have decided that it is not a free market, so surely you have not just a responsibility as you suggest to control it but a responsibility to explain what this new technology is about and the benefits that can accrue to society. Do you not agree?

(*Mr Murphy*) Yes, my Lord Chairman, I do very much so. In those areas where we have specific responsibilities, for example, pesticides and veterinary medicines, we have a much higher profile information dissemination role than in this particular area. We have issued for a number of years now a leaflet on the regulation of pesticides. There is a descriptive booklet issued by the Veterinary Medicines Directorate on their role in the regulation of veterinary drugs. There are many publications in the general food sense series dealing with food safety generally, so in those specific areas where we do have regulatory responsiblity, yes, we do do a lot.

Lord Renwick

157. My Lord Chairman, I should like to ask Mr Murphy whether there have not been some really quite serious problems with pesticides over the years, whether it is GMO or other problems, that have in fact caused a change in the sex of fish or something like that? Is this something that is in your experience and have you had to use your regulatory powers to take action in these areas? Can you give us some details?

(*Mr Murphy*) As I said earlier, my Lord Chairman, there are not any GMO pesticides that are on the market yet. I think your Lordship is referring to what I might term the more conventional pesticides. Yes, it is true that in the past there have been a number of pesticides that have been withdrawn for a variety of reasons, where they have been found to present an environmental hazard or consumer or operator safety hazard. Regulatory action has been taken in that either particular uses for those pesticides have been withdrawn or the pesticides have been withdrawn from the market altogether for all uses.

158. So it is not true that the actual pesticides have produced genetic modification?

(*Mr Murphy*) Not in that sense. I am not aware of that. They have produced adverse environmental or operator or human safety effects. They have caused or they could have caused illness or they could have led to environmental degradation or have had unexpected effects on non target species.

159. But not genetic modification?

(*Mr Bainton*) There may be a problem here in what we mean by genetic modification. In this context, my Lord Chairman, we are using genetic modification as defined by the EC directives, in other words, this is an intended particular manipulation of an organism genetic makeup to change it in a particularly desired way. That does not happen certainly by the use of pesticides, whether deliberately or not deliberately.

Lord Walton of Detchant

160. My Lord Chairman, perhaps I may make a point here. I think that many of the problems of significance to human health relate to a class of organo-phosphorus insecticides, some of which may be very toxic. However, in response to what Lord Renwick said I do not think that any of them produce significant genetic mutation in animals or man, so far as one knows. May I also say in relation to the Food Sense Fact Sheet how much I agree with what Baroness Platt and Lord Wade said about the importance of getting this into the schools. There is a good deal of propaganda aimed at schools, some of it I fear rather biased, about the potential dangers to the environment of several issues and about things such as animal experimentation. I think, for instance, that it is important to have a very clear statement, like this one on "What is Genetic Modification", made available to a very wide audience. Now, My Lord Chairman, may I ask a question out of total ignorance. Supposing you take the Calgene or Zeneca tomato you say that you insert the cloned genes into the actual plant. How do you do it? What is the carrier that is used? I should love to know!

[Lord Walton of Detchant *contd.*]

(*Mr Bainton*) My Lord Chairman, there are various methods of doing this, and you must forgive me because I am not a scientist, so if you really want a very full explanation we will write to you.

Lord Walton of Detchant] Thank you.

Baroness Platt of Writtle

161. Yes, please do.

(*Mr Bainton*) You can use particular strains of bacteria to do this which infect plants.

Lord Walton of Detchant

162. You mean use a bacterial or rural carrier?

(*Mr Bainton*) Or you can use mechanically inserted genes.

Lord Walton of Detchant] The same techniques as are used in animals can be used in plants, thank you, that is all I need to know.

Lord Wade of Chorlton

163. My Lord Chairman, may I come back to something that was mentioned earlier, that is, the fourth hurdle. Can you explain how you understand the need and who will decide what the need is?

(*Mr Murphy*) The concept of the fourth hurdle was explained in earlier evidence, my Lord Chairman. It goes back to the three criteria that are established for the approval of medicines, that is to say, safety, quality and efficacy. The idea of a fourth hurdle first arose in the context of the European Parliament discussion on medicines, and particularly veterinary medicines, where there was a feeling that there ought to be the insertion in addition to the three scientific based criteria of a fourth criterion of need—is there an economic or sociological need? This came up particularly in the context of the use of growth promoters in animal feed. It was mentioned earlier in the evidence of the Department of Trade and Industry that there is a criterion of need in the case of the approval of food additives. That is need expressed in a rather different sense, a technological need—do you need to use a food additive to preserve foods or to give colour, or is this particular food additive necessary because of its colour-giving characteristics or preservative characteristics? It is not altogether easy to separate that concept from one of efficacy, in other words, does it do the job. I think the concept of need in the context of the fourth hurdle discussion in the European Parliament was very much wider. Let me give you an example, that of bovine somatotropin, a hormonal product that is capable of enhancing milk yields in dairy cows by quite considerable factors in excess of 20 per cent in some cases. The question that arose there was, if the product is of satisfactory quality and is safe and efficacious, should it be allowed to be marketed because we have in fact got a surplus of milk in the Community and its use might lead to unemployment in the dairy sectors or it might lead to excessive expenditure on support under the Common Agricultural Policy for dairy production. The concept of need therefore was very much broader there. The argument was, we do not need this product because we have sufficient milk and it will only cause financial or social problems down the road.

164. But does it not concern you that this is very much the Big Brother attitude? How can one group of people decide that another group of people might or might not need something? This is a completely new concept. Does it not frighten you that if you start to go down that route it could lead to this Big Brother attitude of deciding what the rest of us should have?

(*Mr Murphy*) My Lord Chairman, it is a very serious problem and there would be difficulties both in applying the criteria and in terms of the effect that it would have upon industry: it would have very serious implications for innovation in the advanced technology industries and in particular the biotechnology industry. I think that that is why many sectors of the biotechnology industry are very concerned about the possibility of additional regulatory hurdles being created in this form.

165. Is the British Government resisting it?

(*Mr Murphy*) The British Government's policy in general and specifically in the areas in which my department is concerned is to base assessments very much on scientific advice.

Lord Perry of Walton

166. My Lord Chairman, may I say that I am rather horrified that the European Community should even consider the question of the need for milk when in fact the tropical countries in the world have such low yields of milk that the need for this compound world wide is enormous. To use that as a criterion for stopping the production of something seems quite wrong.

(*Mr Murphy*) I should say, my Lord Chairman, that the pressure came essentially from the European Parliament although I think that there are some Member States, in certain sectors at least, who would go along with the concept. In fact, there is at the moment a Community moratorium on the licensing of bovine somatotropin which has been in place for two or three years now and is due to expire at the end of this year. This prohibits Member States from licensing the product.

Chairman

167. We will leave this sordid matter of the Community just for the moment, although I am sure it is very interesting, and go back to one specific item in terms of public awareness and your duties in that respect in so far as you have any. What policy do you have in regard to the labelling of any foods that might have a genetic characteristic?

(*Mr Murphy*) My Lord Chairman, that is an issue that is being currently considered by the Food Advisory Committee. The Food Advisory Committee did issue guidelines over two years ago now indicating how it would proceed in making recommendations to ministers for the labelling of foods produced using genetic modification technology. Those guidelines went out for consultation and the committee has decided that it would like to review those guidelines and consult on a new set of guidelines. It is expected that the consultation document in that area will be issued very shortly. When it is issued, my Lord Chairman,

[Chairman *contd.*]

we will make sure that the Committee receives a copy.

168. What is the view of your department, if you have one, on this? Do you think that labelling should be extended or not?

(*Mr Murphy*) It is very complex, my Lord Chairman. Consumer groups have to a greater or lesser extent expressed views in favour of the labelling of all foods containing or produced by genetically modified organisms. But I have to say, my Lord Chairman, that at a practical level that could lead to major problems. If you take, for example, a genetically modified plant variety, a wheat, or tomato, if you introduced a labelling requirement which said that those tomatoes should be labelled to indicate that they have been produced using genetically modification technology, then that may be reasonably simple as far as the actual tomatoes are concerned, although even then—

Baroness Platt of Writtle

169. But likely to bruise it, I should have thought?

(*Mr Murphy*) There may be problems of that kind, but what about the processed tomato, what about other plant varieties used as foods which go through several processes before they end up in consumer packs? Flour from a modified wheat variety is one particular case, my Lord Chairman. What happens when it is mixed with other varieties of wheat? It is not too fanciful to assume that at some point down the road in a few years' time there will be a large number of genetically modified plant varieties on the market and it may be that they would form the majority of the food in a particular sector, so there are these practical problems. There is also the question of whether there is really a major demand for across the board labelling of genetically modified foods.

Chairman

170. You see to have marshalled most of the arguments, Mr Murphy, but as far as I can see you have not come to a conclusion?

(*Mr Murphy*) I think that the department will await the advice of the Food Advisory Committee in this area, my Lord Chairman, and in giving its advice the Food Advisory Committee will want to take note of the results of the consultation exercise.

Lord Soulsby of Swaffham Prior

171. My Lord Chairman, I was just wondering what you would do with milk derived from a cow that had been protected with a genetically modified vaccine, whether you would have to label that milk—but that is meant more as a joke than anything else. However, I do want to come to the question of manpower, my Lord Chairman. The Department of Trade and Industry obviously expressed concerns about the number of qualified scientists in the field of biotechnology to take up biotechnology in a major way. What is your opinion about this, not in terms of regulation but in terms of doing the basic work and then translating that into industrial production? Are we short of manpower and, if we are, what do you think that we should do about it?

(*Mr Murphy*) In the areas affecting agriculture there are a number of companies involved which have genetic modification programmes. The plant breeding industry is a particular case in point where I think that there is a considerable strength there. In the research area, in universities and research establishments, the last definitive study in that area of which I am aware is the ACOST study of 1990 which did indicate certain strengths, particulary in the plant sciences sector. Within Ministry of Agriculture, Fisheries and Food we have a significant agriculture and food research budget of over one hundred million pounds a year. At our last calculation I think about £15 million was being spent in areas concerned with the new biotechnologies, as defined in their wider sense, and we are currently looking at the possibilities of expanding our involvement in strategic research in the crop molecular biology sector specifically. I think therefore that there are particular strengths that the United Kingdom has that can be expoited. Plant breeding is a case in point.

172. What about the animals side?

(*Mr Murphy*) There are companies active in that area. There may I think be a reluctance to get heavily involved in some areas because of the problems of public acceptability. There is more public concern it seems to me about the genetic modification of animals than of plants so that may be an impediment or may in fact inhibit some work in the animal sector.

Lord Perry of Walton

173. My Lord Chairman, if I may I should like to come back to the question of viability which I raised concerning pesticides. When you consider a genetically modified wheat that will come under the release regulations so it is clearly a viable GMO?

(*Mr Murphy*) That is right, my Lord Chairman.

174. But the bread that is made from the wheat is non viable and is sold in the shops. It seems to me we have to do something to clarify those two things and make it quite clear that the public is at no risk whatsoever and that these are not genetically modified products but made by genetically modified plants.

(*Mr Murphy*) The flour produced by the wheat is not a genetically modified organism but it is the product of genetic modification.

175. And that at the moment falls under the general regulations?

(*Mr Murphy*) No, it does not, my Lord Chairman.

(*Mr Bainton*) My Lord Chairman, the horizontal regulations are concerned with viable organisms. If subsequent processing makes the organism non viable such as the grain from your genetically modified wheat is a potentially viable organism but you put it through the mill and it is no longer a viable organism but the flour and any subsequent product that is made from that flour would not be caught by 90/220 or by the GMO deliberate release regulations but it would eventually be caught by the European Commission's proposal for a novel foods regulation.

Baroness Platt of Writtle

176. If I may just follow up Lord Soulsby's question, my Lord Chairman, I did not detect in the reply, is there sufficient qualified man and woman power in this field, and are the universities, particularly the new ones, producing the sort of people needed and are they then getting the opportunity for practical commercial industrial experience to provide the kind of competitiveness that we obviously need?

(*Mr Murphy*) My Lord Chairman, I do not think that I am qualified to answer that question from the department's point of view. That might be a question that you need to put to another department, perhaps the Department for Education or the Office of Public Service and Science.

Chairman] Thank you very much, Mr Murphy and Mr Bainton. If there is any further information that you wish to let us have we will be very pleased to receive it. Thank you both for coming.

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SESSION 1992-93

MINUTES OF EVIDENCE
TAKEN BEFORE

THE SELECT COMMITTEE ON SCIENCE AND TECHNOLOGY

Thursday 1 April 1993

ZENECA

Dr [illegible], Mr C [illegible] and Professor [illegible]

GLAXO GROUP RESEARCH LIMITED

Dr [illegible] and Dr M [illegible]

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HOUSE OF LORDS SESSION 1992-93

MINUTES OF EVIDENCE
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THE SELECT COMMITTEE ON SCIENCE AND TECHNOLOGY II

Thursday 1 April 1993

ZENECA

Dr E Dart, Mr G Musker and Professor N J Poole

GLAXO GROUP RESEARCH LIMITED

Dr J B Ward and Dr M Weir

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THURSDAY 1 APRIL 1993

Present:

Flowers, L.	Renwick, L.
Hilton of Eggardon, B.	Soulsby of Swaffham Prior, L.
Howie of Troon, L. (Chairman)	Whaddon, L.
Perry of Walton, L.	

Written Evidence from Zeneca

1. *What is your interest in biotechnology?*

Zeneca is a fully owned subsidiary of ICI and has four businesses (pharmaceuticals, agrochemicals, seeds and speciality products) which are fully involved in exploiting the opportunities offered by biotechnology. The company employs 33,000 people and had sales of almost £4 billion in 1992. Zeneca invests heavily in the research and development of new products, the enhancement of its existing range and the improvement of manufacturing efficiency. Biotechnology is a fast moving area of research which provides a unique set of tools which Zeneca is making full use of in each of its businesses. In 1992 Zeneca spent £457 million and employed 7,000 staff on research and development; the majority of this expenditure was in the U.K. The extent of Zeneca's use of biotechnology is illustrated in the article reproduced as Annex 1. (*not printed*)

2. *How and why is biotechnology important to U.K. industry?*

In the coming years biotechnology offers opportunities for economic growth in the health care, chemical, agricultural and food sectors. These are sectors where British industry has traditional strengths, and which make a significant contribution to the wealth of our country. In the next decade the British consumer will increasingly be offered, and will also demand, products which have been produced using biotechnological techniques; it is essential for the future prosperity and prestige of this country that as many of these products as possible are developed and manufactured by U.K. industry.

3. *What future prospects and opportunities does the technology offer?*

The techniques embraced by the term biotechnology will be the next major source of innovation in the above mentioned industries.

The invention of new drugs, agrochemicals or the breeding of new plant varieties in the 1990s requires, more than ever, a molecular insight into the functioning of genes, cells and tissues. The skills of those trained in biotechnological techniques now complement the established research disciplines in the pursuit of effective solutions to the challenges facing our society. These challenges include finding cures for cancer and diseases of the ageing, reducing the environmental impact of our activities or providing better quality food.

4. *Which developments in biotechnology raise issues of safety and how should they be addressed?*

Our ability to transfer genetic material between different species (genetic modification) and the ability of these genetically modified organisms (GMOs) to self-replicate is often cited as a cause of concern, for example that man will inadvertently create new pathogens or weeds. We find arguments that genetic modification is inherently safe are as unhelpful as arguments that all genetic modification is dangerous and should be stopped. What society needs is a science based regulatory system, that is strictly enforced by a regulatory authority. Such a system would encourage research and investment and would help develop the confidence of the public.

We believe that the U.K. until the late 1980s was developing a regulatory system that protected both man and the environment while encouraging investment in research and industry. However, the debate over the last few years on the implementation of European Directives 90/219 and 90/220 has impeded the conduct of research and development in both academic and industrial sectors and there is no evidence that safety has been increased. This is because the Directives appear to be based on the concept that genetic modification *per se* poses unique risks to man and the environment and therefore must be controlled in a unique manner. In addition to the damage to our academic and industrial competitiveness, the debate has done nothing to build public confidence in the regulatory system. We develop these arguments in the following sections.

The design of the risk assessment procedure is fundamental as this will establish the type of controls needed. We believe that assessment of risk should:

- Recognise that genetic modification work on viruses, bacteria, fungi, plants or animals poses different potential safety issues because these organisms are so different from each other.
- Accept that work during the research, development and commercialisation phases or in a laboratory, factory, glasshouse or field trials, poses many different potential safety issues.

- Build up confidence on a case-by-case approach with a combination of risk assessment and monitoring.
- Take account of existing knowledge, for example, about the usual behaviour of crop plants.
- Acknowledge the considerable body of experience gained by successful genetic and modification work.
- Be concerned with the objectively measurable criteria of safety, quality and efficacy.

The above would allow rapid progress to a situation where regulatory attention and resources could be focused upon developments which pose a real risk.

Over nearly 20 years, genetic modification in the U.K. and world-wide has had an exemplary safety record. Where safety issues arose during the application of the technology, for example during discovery research or process development, then they were handled effectively and safely by existing legislation. Examples of such legislation are the Health and Safety at Work Act (HASAWA), the Control of Substances Hazardous to Health Regulation (COSHH) or the Genetically Modified Organism Regulations of 1989. When safety issues arose with a product which was also a GMO then the appropriate product regulations were applicable.

We believe that for the United Kingdom the Advisory Committee system has proved to be an effective way of regulating biotechnology. The Advisory Committees for Genetic Modification (ACGM), Release into the Environment (ACRE) and Novel Foods and Processes (ACNFP) have provided a forum where scientific advice can be gathered and the evidence concerning a particular issue reviewed by a broad representation including "lay" involvement (representatives of the employers, trade unions, local government etc.) Such experience would develop along the lines of work with unmodified organisms, which are controlled by the Advisory Committee for Dangerous Pathogens (ACDP) guidelines. It is interesting to note that these guidelines are less restrictive than the new Genetically Modified Organisms (contained use) Regulations despite the fact that genetic modification work is normally based on non-pathogenic micro-organisms and known gene sequences of known properties.

5. *Should biotechnology be regulated by an industry specific regime?*

There is no such entity as a biotechnology industry, therefore there is no need for a biotechnology industry specific regulatory regime. However, there are sectorial industries which employ biotechnology and are already regulated for safety, quality and efficacy. For example, genetic modification may be used in the production of, flowers, potato tubers, yoghurt, bread, potato crisps, anti-rabies vaccine, anti-cancer drugs. Each of these products raises its own safety questions. It is therefore in our view axiomatic that each class of products requires its own specific evaluation and should hence be regulated by the appropriate specific regulatory regime. These sectorial based regulations will of course evolve to accommodate new technology if it changes the essential nature of the product.

6. *From a technical point of view, is horizontal regulation (where a product is judged through the process by which it is derived) better than a vertical regulation (where a product is judged by its characteristics)?*

The key question is whether the trigger for the regulatory review should be the act of genetic modification or the product. There are three broad areas for regulation: laboratory research, the development period (trials etc.) and placing a product on the market. The first can be realistically handled by regulations concerned with protection of the worker and, if appropriate, protection of the environment. However, once one has actually used the techniques to produce a potential product then there is a clear difference of opinion on how to regulate. The European Community produced Directive 90/220 which uses as a trigger for regulatory review the act of genetic modification. In the USA existing legislation was adapted to deal with the development and marketing of products produced by genetic modification.

The vast majority of scientific opinion supports the product approach. For example:

In Ecology (1989), 70, 297-315, prominent ecologists summarised the critical issues surrounding the release of genetically modified organisms. One of their key recommendations was that GMOs "should be evaluated and regulated according to their biological properties (phenotypes), rather than according to the genetic techniques used to produce them".

Brill in "Issues in Science and Technology" (1988) notes that we have considerable experience with organisms that are modified by traditional techniques. In most cases the nature of the genetic modification achieved by these traditional techniques has been far more dramatic than that accomplished by recombinant DNA technology.

The National Research Council (1989) published a report on Field Testing of genetically Modified Organisms. For crop plants they concluded that "crops modified by molecular and cellular methods should pose risks no different from those modified by classical genetic methods for similar traits. As the molecular methods are more specific, users of these methods will be more certain about the traits they introduce into the plants. Traits that are unfamiliar in a specific plant will require careful evaluation in small-scale field tests where plants exhibiting undesirable phenotypes can be destroyed." The paper also proposes that as our knowledge increases, entire classes of introductions (of GMOs) may become familiar enough to require minimal oversight.

Super-imposing a horizontal regulatory approach upon a vertical regulatory system will not lead to any increase in safety for human health nor in the environment.

7. *Should regulation evolve from a horizontal to a vertical approach in each industrial or environmental application?*

Horizontal regulations are appropriate where the application of a technology raises safety issues. Vertical regulation is appropriate where the product is being developed or commercialised.

In the medicinal product sector, it is hoped that the EEC will follow the USA model to a degree by permitting the assessment of safety under 90/220 to be conducted by the medicines agency as a part of the assessment under the medicines directives.

Gene therapy offers considerable benefits in the treatment of diseases. Over the last five years there has been an extensive review of the technical, safety and ethical issues concerning gene therapy both in the USA and in the EC. Currently, there are stringent regulations governing the application of somatic gene therapy. We believe that any relaxation of these regulations will depend on the experience gained from the first batch of trials. Zeneca endorses this regulatory approach.

8. *How do current regulations compare with those of competitor countries*

In 1990 the EEC passed two Directives covering biotechnology: one for contained use of GMOs (90/219), the other for the deliberate release to the environment and marketing of GMOs (90/220). However, the EEC Communication "Promoting the Competitive Environment for the Industrial Activities Based on Biotechnology Within the Community" which defines the policy for biotechnology in Europe and hence the role of regulation has not yet been debated in the European Parliament. Member States should have implemented Directives 90/219 and 90/220 into National legislation by October 1991. Many Member States are finding it difficult to implement these Directives. In the U.K. the regulations which implement the Directives had to undergo extensive modification after the first round of consultation because of their inappropriate and grossly convoluted format.

It is valuable to contrast the development of the two major regulatory influences on biotherapeutic manufacturing in the U.K., ie the European Guidelines on Good Manufacturing Practice and the EC Directive 90/219 on the contained use of genetically modified organisms. The former regulations evolved over 30 years through close co-operation between the pharmaceutical industry and the regulatory authorities. Standards in concept, design and engineering practice have been developed which are universally recognised and accepted. On the other hand, the new regulations on containment of processes involving recombinant organisms which have been imposed on the industry, are sufficiently vague in defining what is actually required in practice to cause uncertainty.

The Directive 90/220 imposes a horizontal based regulatory approach on the commercialisation of products. This approach has inevitably led to arguments over:—

- definitions, ie what actually is, or is not, meant by genetic modification
- excessive bureaucracy, though at last there are some discussions between the European Commission and Member States to develop "simplified procedures" for the Deliberate Release Directive which will try and remove unnecessary regulatory burdens for certain types of genetically modified crop plant. These changes are occurring even though the Directives have not been implemented in all Member States.
- conflicts with existing vertical regulations which is leading to the rewriting of vertical regulations and directives in an attempt to develop a workable vertical or product-based system. For example, we understand that Directives or Regulations on Patents, Novel Food Ingredients, marketing of Genetically Modified Farm Animals, marketing of New Varieties of Plants, Transport of Genetically Modified Organisms are now being prepared. Simply transferring the requirements of Directive 90/220 into vertical regulation may be an administrative solution, but we fear that this will be a case of "building a house upon the sand".

The complexity of, and the confusion, caused by these Directives is sending a very negative message to the academic, industrial and financial communities. More seriously public confidence in the regulatory systems is being damaged.

Special legislation for regulating genetic modification was not developed in the USA. Their regulatory system is based on existing legislation which covers, for example crop plants and food, the logic for their approach is outlined above. This has had two advantages:—

- the degree of regulatory oversight can be easily modulated in the light of experience.
- there is no disruption of the existing product legislation.

The result is that both the industry, and in our experience the majority of the public have confidence in the regulatory system

The United States Department of Agriculture has recently, after holding public hearings, proposed that the present system requiring permits issued by the USDA should be replaced by a notification system for field trials with certain crops (corn (maize), cotton, potato, soybean, tobacco and tomato) when the genetic material inserted is well characterised.

In essence, although U.K. biotechnology regulation is seen to be at neither extreme of the implementation of 90/219 and 90/220 in Europe, European biotechnology overall is greatly disadvantaged with against that of USA and Japan.

9. *What are the consequences, or likely consequences, of the regulatory regime on competitiveness of the U.K. industry, in particular as regards*

1. *research*
2. *product development*
3. *investment*
4. *location*
5. *sales and marketing?*

Zeneca Pharmaceuticals currently estimates that its genetic modification safety costs will rise by approximately 50 per cent to meet the new regulations. Additional capital expenditure of 5—10 per cent is required for normal research activities, while this will rise to 25–30 per cent for certain larger scale activities. Similar costings are predicted by the other Zeneca businesses.

At the present time, Zeneca Pharmaceuticals is producing all material for clinical and preclinical testing within the U.K. either in-house or through contractual arrangements. Where Zeneca will manufacture in the future has not been decided. It is, however, clear that the evolving regulatory climate and attitudes in European Community will make a significant contribution to this decision. For example, in Germany difficulties on the regulatory front have led several companies to build their facilities in the USA. The incoming investment that is being attracted into Europe is, at the moment, largely going outside the U.K.: in particular to the Republic of Ireland and to the Netherlands.

Zeneca Seeds carries out research in Argentina, Belgium, U.K. and the USA and has carried out field trials with genetically modified crop plants in Australia, Belgium, Canada, Chile, U.K. and USA (California, Florida and Iowa). There is an increasing cost of carrying out field trials in the U.K. For example, to obtain permission for a four hectare field trial in California requires under 25 per cent of the paper work required for a 400 square metres field trial of oilseed rape in the U.K. As noted above when the proposed USDA system is adopted a notification letter will be all that is required for the American field trials.

10. *Is there a danger that the present regulatory regime will prevent the exploitation by British industry of research conducted in the U.K. science base?*

The U.K. biotechnology research base has been first rate and industry is developing many of its ideas. For example, some of the research at the Universities of Cambridge, Edinburgh, Leicester, Nottingham, Oxford and Warwick has been, or is being, developed by Zeneca. This research is creating jobs and wealth in the U.K.

We would like to repeat part of the summary of the views expressed by ICI on the forthcoming Government White Paper on Science and Technology.

> "Innovation for World Markets is needed to prevent terminal decline of U.K. manufacturing industry.
>
> Leaving aside all special pleading, the U.K. science base is substantially underfunded.
>
> We cannot afford everything and must give greater reinforcement to those areas of science and technology which are inherently more exploitable and where we have some sort of national advantage."

In the biotechnology area the U.K. has a commendable record of both research and industrial achievement. From the above paragraphs it is clear that we have serious concerns that the costs associated with over-bureaucratic regulations in the U.K. and Europe will damage University research. This will make the U.K. a less attractive prospect in the future for companies such as Zeneca.

11. *How best can issues of public acceptance be addressed?*

The public perception of biotechnology varies considerably from country to country and between product sector.

Biotechnology will not be used by British industry if society or the consumer does not want the resulting products. The question is, therefore how to provide the public with the information they need to make a decision.

Non-governmental organisations have a role to play and industry, university and research institute scientists must be prepared to provide the answers to their questions. We have found dialogue with many of these groups to be very productive. However, we have to accept that there are some extreme pressure groups who are simply opposed to biotechnology. In the U.K. these extreme groups have not yet had the degree of negative influence on the image of biotechnology that has been achieved by their counterparts in, for instance, Germany. Were the lobbying and scare-mongering of the extreme pressure groups in the U.K. to gain the upper hand then doubtless the serious problems being faced by academia and industry in Germany would occur here.

In order to encourage public confidence there is a need for a focused campaign aimed at explaining to the public in honest, non-scientific terms the technology, the regulatory safeguards and the benefits arising from each sector of biotechnology. There is also the need for a source of information which in the view of the public offers a factual and unbiased service. We believe that this is the role of organisations such as the COPUS, the Science Museum and the National Centre for Biotechnology Education at the University of Reading; these organisations require government funding.

Regulation has a critical function to perform in this context. The right level of regulation will reassure the public but inappropriate regulation would not satisfy public confidence and would severely damage the efforts and prospects of those industries where biotechnology is an ever increasingly important tool.

12. *What other factors do you consider will play a crucial role in the competitiveness of the U.K. biotechnology industry?*

Beside the impact of an excessively bureaucratic regulatory regime in the U.K. we consider that the following factors are also undermining the future competitiveness of our activities which are dependent on the application of Biotechnology:

(a) Intellectual property rights:

The genetic modification of organisms has raised a number of new issues regarding patent rights. The main problem at present is that very broad claims are being granted by the European Patent Office (EPO); it is difficult to see how these broad claims are justified by the actual invention made by the patentee. This means that the rest of industry is held up by those claims unless licenses are granted. Improved training of examiners at the EPO in this fairly new area of technology could help to avoid this problem: though, more fundamentally there is a question of whether the EPO's approach gives the proper balance between the rights of the patentee and those of the public.

A problem of unfair competition which is not unique to biotechnology is the US practice of granting claims to the first party to *invent in the USA*, which places non-US inventors at a significant disadvantage: but there are prospects that this will be resolved by a Patent Harmonization Treaty.

The Directive concerned with the patenting of biotechnological inventions has been the cause of extensive debate in the European Parliament and is now in the hands of the Council. Zeneca needs legislation which offers adequate protection for our large research investment in biotechnology research. The general response of industry to the proposed legislation is that it fails to achieve this, and indeed would create damaging precedents with Farmer's privilege and compulsory licensing; it also does not conform to the current GATT-TRIPS proposals.

(b) Funding of basic research:

Historically the U.K. has much of which to be proud in regard to the basic discoveries which have stimulated modern biotechnology. The structure of DNA, the unravelling of the genetic code and the discovery of monoclonal antibodies are attributed to U.K. laboratories. As noted above, Zeneca seeks to work with Universities in basic research in the belief that this will lead to innovative products. Basic research is very costly and it is imperative that the U.K. ensures adequate support for this work either directly or through effective competition for EC programme funds.

(c) Education:

The creation of an increased level of awareness in schools and universities of the positive contributions of biotechnology to health and national prosperity will achieve two critical goals. Firstly it should help to counteract any fear of biotechnology that arises through ignorance within society at large. Secondly it is essential to support the creation of an adequately trained scientific workforce to deliver what we hope will be a significant contribution to the U.K. economy from the application of biotechnology.

Examination of witnesses

DR ED DART, Zeneca Seeds Research Director, MR G MUSKER, Company Secretary and PROFESSOR N J POOLE, External and Regulatory Affairs Manager, Zeneca Seeds, called in and examined.

Chairman

177. Good morning, gentlemen. Welcome. I think some of us had the pleasure of meeting some of you down at Jeallot's Hill a few weeks ago where you gave us a very full presentation of these matters. Would you like to say something to us in general, introducing your colleagues, Dr Dart?

(*Dr Dart*) Thank you very much, Lord Howie. My Lords and Ladies, we are delighted as Zeneca to be given the opportunity to speak to you today. I would like to start by introducing my two colleagues here: Dr Nigel Poole who is the Regulatory and External Affairs Manager for Zeneca Seeds who has a lot to do with biotech regulatory issues and Mr Graeme Musker who is the Zeneca Company Secretary, who is here to keep us honest! I am research director of Zeneca Seeds but also play a role in co-ordinating biotechnology across all of our bioscience research. As you will see from our submission the biologically based businesses in Zeneca cover pharmaceuticals, crop protection, seeds and biological products. Biological products cover applications of biotechnology outside of the health care and agricultural fields. We believe biotechnology is vital to the development of all of these business. In pharmaceuticals it gives us access to or the option to create new protein drugs. Worthy of mention here is one in Phase I clinical development for the treatment of colorectal cancer which at the moment is a non treatable disease. In our view the main impact of biotechnology in pharmaceuticals will be in facilitating the invention of new synthetic small molecules drugs through greater understanding of biological systems and in designing smart screening procedures that will help us identify more active molecules in a more efficient way. In crop protection the story is somewhat similar. We are interested in the isolation and design of biological control agents for some pest and disease applications but also in using the extra understanding that the new bioscience techniques give us to help us design new synthetic active ingredients that are safer, used in lower doses and more environmentally friendly than those currently in use. In seeds we entered the business in the belief that the plant breeding process was going to be changed by the application of biotechnology both in making selection more efficient and in helping the plant breeder to have access to novel sources of genes. We believe both of these aspirations are coming true. In our biological products business we have products like Quorn, our microprotein processing foodstuff—which some of you tasted when you visited—and Biopol, a biodegradable plastic. We also use biological systems to make molecules that organic chemists find it difficult to make in economic amounts themselves by a process called biotransformation. We are also interested in the use of micro-organisms as what are called bioremediation agents, for cleaning up contaminated waste and soils. So as you can see we have a fairly extensive interest in the technology. Alongside this we have made contributions to the developments of GMO regulations in the United Kingdom. ICI and Zeneca has always had representatives on the Advisory Committee of Genetic Manipulation and its precursor groups. We also have representation on the Advisory Committee on Release to the Environment and the Advisory Committee on Novel Foods and Processes. We have always been impressed by the way that these groups have managed the evolution of the technology and balanced it with perceived risk. Our concerns began when the European Commission introduced its Directive 219/220 and in our view did not give credence to the views of experts in this industry. We were then not organised as a European industry to give a collective response to 219 and 220. To ensure our collective voice was heard we and other major European companies, with the agreement of the rest of the European industry, formed the Senior Advisory Group on Biotechnology whose aim was to ensure that the Commission was aware of industry's concerns in developing biotechnology regulations. Dr Poole will say more on SAGB later. Our stance on regulations is that we need them. If Government were not to have them we would impose them on ourselves. But in our view regulations have to be soundly scientifically based and should evolve in a more or a less stringent way depending on how experience develops. In summary I would say this technology is of great importance to us and we believe both to us and to Europe's economy. It offers us novel cures to difficult diseases like cancer, Alzheimers and arthritis and the prospect of correcting genetic defects. In agriculture we can see prospects for crops with enhanced quality and resistance to stress, pests and diseases as well as offering new strategies for crop protection. The prospect is also there for the extension of agriculture to producing novel feedstocks and products for both the chemical and food industries. So it is a technology that we are excited about but we are determined that we will progress under the regulatory regimes that are imposed by the various governments of the world. That is all I would like to say as an introduction.

178. Thank you. Before we go into detail, can I ask you a general question: I am told the DTI has established seven de-regulation task forces of one sort or another. I think one of them at least impinges on your area of activity, are you aware of this and do you intend to make any submissions to the task force?

(*Dr Dart*) Perhaps Dr Poole can answer after me but we are aware that these task forces are set up and we are delighted that there is a watchdog on the regulator, if you like, because I do think that is a very important thing to have so regulations do change with the way that perceived risks develop. We have not as yet decided whether or not to make a submission to this group.

(*Professor Poole*) Just one point about the name, we are not looking for no regulations, we are looking for the appropriate level of regulations. We shall make evidence I am sure when asked.

[**Chairman** *Cont*]

179. When you make submissions for consents and so on, do you get any help from the DoE or the Health and Safety Executive in drawing up your submissions?

(*Dr Dart*) To, for example, the DTI?

180. Yes?

(*Professor Poole*) Submissions to do an experiment?

181. Yes?

(*Professor Poole*) We find the Health and Safety Executive and the DoE are very helpful, you know who to ring up and they will give you advice and we take it.

182. Do you discuss your submission with them before you put it in?

(*Professor Poole*) We try to understand the questions to be asked and the answers, then we put together our submission, then it is up to the DoE and HSE to progress it.

183. You mentioned SAGB, could you tell me what it is and what its achievements are?

(*Professor Poole*) As you have seen from our submission one of our arguments is that biotechnology is a set of tools which covers a very wide range of sectors, four or five sectors in our business alone. The problem then is that there is a large number of industrial associations and federations both in the Member States and in Brussels, all interested in biotechnology. The message we got from the Commission and from our own soundings was that we needed a co-ordinated voice. So the SAGB was formed three or four years ago with the objective of providing that senior umbrella organisation to provide that brief. Its functions are to co-ordinate input into the Commission and to the Council of the right sector groups so they know who to ask and to call in effect. It is clear from our submission—and I am sure the submissions of other companies—that biotechnology is the next driving force for innovation in the European industry. I think the SAGB can claim some success for that realisation which is dawning in the Commission of the importance of biotechnology. We saw that a year ago with the publication of the policy of biotechnology for European industry. I think there are other things about SAGB. As we are all moving towards the new Europe, the new Single Market, industry is having to learn how to relate to the European institutions and the SAGB is an experiment in how to relate to the European institutions and I think a very successful one. It is a model which has been followed in other sectors already. I think it has also helped bring some of the expertise into the Commission and into the Council. We have been able to identify people who know what the subject is and they have been able to help advise the Commission so I think it has helped the Commission as well.

184. You think it is a thoroughly useful body then?

(*Professor Poole*) It has been an extremely useful body, yes.

(*Dr Dart*) I think part of the measure of that is it started with seven large European companies and the membership now is what, Nigel?

(*Professor Poole*) It is about 34 large and small companies. It is not an association of everybody, it is an association of companies who are doing major research or development in the European Community so it is large and small companies and all Member States.

(*Dr Dart*) And a waiting list I gather?

(*Professor Poole*) And a waiting list.

185. Biotechnology is thought to offer some risks to health and the environment, what risks do you see?

(*Dr Dart*) I must stress at the outset that all the risks are perceived, in 20 years of operation of this technology there is no known risk that has developed as a result of the technology. I would break this into several categories. There are risks associated with the worry about creating the dangerous pathogen from something that was not a pathogen to start with and that is why the containment regulations are there. I was involved in some of the early debates in this and I can remember an experiment that Professor Ken Murray did because at the time they were thinking what is the most dangerous experiment we can conceive of and let us test it under high containment conditions. What they conceived of was inserting genes that caused cancer into a Mouse via the *bacterium E.coli*. These were the polyoma virus genes. So they put the genes into *E.coli*, fed the *E.coli* to mice, and asked whether the mice developed a polyoma derived tumour. The answer was no, in fact it was a safer way to look at and examine these genes, putting them into *E.coli*, rather than handling them separately. The mice did not get cancer. In fact, you could not even pick up any live genetically modified *E.coli* in the stools of those animals. That was one of the first indications that most of the laboratory organisms that people are working with are either disabled or incapable of competing in the wild. That is not to say that there will be some risks in some organisms. That is why the Advisory Committee on Genetic Manipulation exists, to monitor experiments. Nonetheless, this was one of the early concerns and explains why laboratory containment should be appropriate to the nature of the perceived risk. In fact, risk categories have changed as people have got more confident of what is potentially a risk and what is not.

Lord Perry of Walton

186. That in itself is an example of what is called horizontal regulation. There is nothing wrong with horizontal regulation at the laboratory stage.

(*Dr Dart*) Exactly, I totally agree. If I can move on to other risks in my sector. One that is always expressed as a concern is the chance in a plant breeding programme of creating a weed species out of something that was not by the act of genetic manipulation. What people actually do not realise is that a plant breeder is selecting from massive populations of plants for a set of defined characters of which yield and quality are both important and we would naturally reject anything through this process. A character like weediness is very, very complicated genetically and to actually create weediness by introducing one or two genes is almost impossible. If I were a plant breeder, and in fact I am responsible for a lot of them, I would be quite offended by any implication that I could inadvertently create a weed.

[Lord Perry of Walton *Cont***]**
Most of the things I am creating are incapable of competing with the wild species in the environment and are only capable of delivering the effects the farmer wants. Nonetheless, the sorts of checks and balances that we have in these guidelines will always pick those sorts of things up. Another question has been genetic stability: if we put these constructs into a plant will they be stable, is there something funny about Recombinant DNA that creates some instability in the wild? Again the answer is plant breeders are in the business of supplying stable genetics to the customer and they go through seven years of testing to make sure that they are genetically stable. That has nothing to do with regulations, that is to do with the fact that they are selling seeds to the customer and if that seed is not stable they will lose the business.

Chairman

187. Do you not see it as a very risky business?
(*Dr Dart*) No, I do not see those sorts of things as a risky business but there are some that are actually implying that they are and I do not think they have the background of what goes on in those industries now to look at them.

188. Do you think the existing regulations offer sufficient protection against any—
(*Dr Dart*) Yes, I do. Yes I do, very much so.

Lord Perry of Walton

189. Can I ask another question? You have mentioned in passing two different, to me they seem very different, kinds of product, one is a viable GMO and the other is a non-viable protein or other pure chemical that can be released. Is there a reason for rewriting the regulations to cover these two things in different ways?
(*Dr Dart*) I do not think so. I think you need to deal with it more about perceived risk than viability of the GMO. Let me give you an example of something that we have been wrestling with in this horizontal/vertical debate. We are interested in producing improved tomatoes in various ways. I have been quite fascinated by some of the debates going on in this area. Most of what we are doing through Recombinant DNA technology could be achieved through the traditional breeding techniques but it would take longer. For example, you see on the shelves now yellow tomatoes, nobody buys them and it is no big deal commercially but those yellow tomatoes have been selected by standard natural selection procedures. That is a mutation in the tomato that stops it at yellow. Through recombinant technology we can create the same effect, exactly the same effect more efficiently. So you say: "Well what is the difference there between using this technology in a more efficient way and something that could have been produced already?" They are both viable GMOs.

Lord Whaddon

190. Neither of them sell?
(*Dr Dart*) In that case neither of them sell but I can give you examples of others. I thought I would use that one, it illustrates something around already, I will give you another if you like?

Lord Perry of Walton

191. The worries of the public may be quite unnecessary but they are there.
(*Dr Dart*) Yes.

192. It seems to me the worries need not be there at all for the non viable products of GMO.
(*Dr Dart*) Yes.

193. Whereas you cannot really wipe the worries about viable GMOs out completely?
(*Dr Dart*) Yes.

194. It seems to me we would take a step further, would you agree, if we were to divide the two up that way?
(*Dr Dart*) That is one division but I think there is another division as well which is to do with of the viable ones which ones are we relaxed about and which ones are we concerned about?

195. Risk assessment?
(*Dr Dart*) Which is risk assessment. The USDA have done this brilliantly in my view, they have had experts look at six major crops and try to conceive of every risk scenario and decide whether these crops fall into a low or a high risk category. For example, corn and soya beans are going to be the basis of a very simple procedure.

Chairman

196. These regulations you believe offer adequate protection to the public, how do they affect your business? Do they restrain your competitiveness in any way?
(*Dr Dart*) I believe that the regulations derived from the current directives, they are a bit of a lead ball at our feet compared with what we see in other parts of the world.
(*Professor Poole*) I think the concern with the European approach is we have set directives in place which have to be implemented at the national level which makes the statement that genetic manipulation is by definition dangerous and needs to be regulated. It is a horizontal regulation which covers everything from the research phase to placing on the market. We are worried about this for three reasons. The first reason is, Dr Dart talked about producing the same product by two different techniques, now if one of those products is covered by horizontal legislation and the other is not, you are actually getting two standards. That is not in our interest and it is not in society's interest to have two standards. The answer we believe is as soon as you have done your transformation and you have started to develop and then market your product, you go into vertical legislation which exists for all products and the skills to handle the risks and the benefits are actually within that vertical legislation. So, for example, if it is a vaccine and you are concerned about shedding the vaccinia into the environment, the lead should come from the Department of Health, that is where the expertise lies. If it is a tomato it is the Ministry of Agriculture, Fisheries and Food. What we are seeing here is this confusion developing between horizontal and vertical not at the laboratory stage, not at the

[**Chairman** *Cont*]

research stage but at the stage of development and marketing. We are worried about this duplication of standards. Another problem is that it is actually diluting effort. We are having to put in sometimes two dossiers to two different departments. We are putting scarce resources, and the Government resources as well, on to low prioirty areas rather than those that would require more scrutiny. I think also we are seeing increasing dissatisfaction or confusion about the role of vertical regulation, not just the GMOs but the non GMOs as well. Already in Brussels we understand they are writing new directives and new regulations to cover transport, to cover marketing of all genetically modified animals, to cover marketing of genetically modified plants, to cover pharmaceuticals, to cover patents. Only in Europe do we see this job creation scheme going on. The danger of it is it is affecting the whole regulatory system in Europe. Our system depends on trust by ourselves and by the regulators and by the public.

Lord Flowers

197. Is Professor Poole saying it is the bureaucratic rather than the technological aspects of regulation as having to be practised by you at present that causes you the greatest concern?

(*Professor Poole*) It is the over-bureaucracy, Lord Flowers, yes.

Lord Soulsby of Swaffham Prior

198. You mentioned the word trust on the part of the public but I would like to go back briefly to this question of competition between what we might call the wild or the normal plant and the genetically modified. While one might accept the competition on the one to one basis would be very much in favour of the wild plant, might there be a quantitative situation here that if the natural is overwhelmed by the genetically modified that the genetically modified might take over.

(*Professor Poole*) Yes.

199. I think that is the sort of worry the public might have, not that they do not believe you but they do not believe you can see far enough ahead in terms of quantitative situations.

(*Dr Dart*) I appreciate that is a public concern and one problem we have is trying to get the public to have a feel for what crop plants are like in competitiveness. There was an experiment I recall done I forget how many decades ago at Rothamptstead where they planted a field of wheat and they said: "Let us let it go fallow now and see, it might be 15 years time but let us have a look and see what happens to it". It finished up as a wood and there was no detectable wheat. What that is telling us is that the crops bred by man do not have the capability of competing with wild populations. If you add to that the fact you are putting one or two genes into this crop to create the disease resistance or whatever, how are those going to change the competitiveness of those plants so they can outstrip the woods? I find it very difficult to foresee how that would happen but that is what the regulatory authority should be there for. It is saying: "Okay you have put in the genes for resistance to a fungus or something, does that change its competitiveness or does it not?" That is something plant breeders can test for anyway and they have got many years to test for it anyway. I think that is a reassuring check at the end of a lengthy process.

Lord Perry of Walton

200. Can I come back to what Lord Flowers was saying about bureaucracy. There is a lot of talk in the submissions we get about the interpretation of the regulations and how it can vary. Does bureaucracy mean they are being interpreted wrongly or not sufficiently simply? Could they be interpreted in a different way by the British regulatory authorities so they became an acceptable and an easy way of handling it?

(*Dr Dart*) My answer to that, I think, Lord Perry would be yes. If I look at the US system which I was referring to earlier they have already decided that there are some crops which present minimal hazard and will require a notification procedure. We have just heard this morning it is going to be two pages and 30 days' notice to do experiments in those crops because they have been through the debate about the risks there. I would hope in Europe we move to some system that is like that where for some areas of low perceived risk we move to simplify procedures.

201. That would be presumably within the regulations as they exist without amendment?

(*Dr Dart*) That is a good question. We are certainly hearing the regulatory people telling us that is a possibility but we have yet to see it in action.

Lord Renwick

202. You do find good communication with the regulators and you do find that they are not written in stone, you do find they do think as the technology develops and knowledge of technology and the implications of the technology that the regulations could be changed to the favour of the competitiveness of the industry?

(*Dr Dart*) I think at the moment the dialogue with the regulators in the United Kingdom has been very good. I think our concern is how that dialogue gets translated into Brussels and whether Brussels will really listen.

Lord Flowers

203. Can I ask a slightly different question: in order to get some sort of measure of how burdensome you find biotechnology regulation, you are regulated in all sorts of other ways? You are audited, for example, you have ordinary health and safety regulations, innumerable things, regrettably perhaps, how burdensome is biotechnology regulation?

(*Dr Dart*) That is a difficult question because it is a bit apples and oranges, if you like. You know in the health care area the regulations and development of a drug are massively expensive and if that happened in my sector it would just totally render that sector uneconomic and also it would not be balanced with the perceived risk in my view. So compared with things like that, you would have to say these regulations are not onerous. You have got to look at it within the costs of the sector you are dealing with and the risks within that sector.

Lord Perry of Walton

204. If you take one of your medical proteins, will that not have to go through the Safety of Drugs Committee after it has gone through these regulations?

(*Dr Dart*) Yes. That is your horizontal and your vertical.

205. That would be a duplication?

(*Dr Dart*) Yes.

206. Would you argue that you want to cut out the GMO regulations and go for the Safety of Drugs' regulations?

(*Dr Dart*) Yes. My argument would be, as I think you said earlier, at the laboratory phase there is no problem about horizontal regulations. There is a stage when you move into development and marketing when it ought to go down the track where the most competent people can judge whether it should be marketed. I would say in the drug area it is the Safety of Medicines and in the agricultural area it is MAFF. MAFF look after pesticides now and they also look after the registration of plants.

207. The reason I asked the question about viable and non-viable is that in the drug area we normally are thinking of the non-viable . There may be an occasional viable application to man although I do not know them yet.

(*Dr Dart*) Yes.

208. In that case it might not fit into the Safety of Drugs' regulations. That was the reason for my question.

(*Dr Dart*) I see, yes.

Lord Whaddon

209. There are large parts of the world where there are no regulations at all at the moment. Have you any knowledge of any research emigrating to those areas and are there any risks that you know of due to the fact that there are areas of the world with no regulations? If so, what do you do about it?

(*Dr Dart*) If I can start and perhaps then pass it on to Nigel. We have had this problem already because we wanted to do a bulk up of genetically modified tomato seeds in Chile, in a winter nursery sense to bulk up for the next summer in America. The problem we faced was that Chile did not have any regulations. What we decided as a policy was to apply the same regulations to ourselves in Chile as we would in the United Kingdom but we would talk to the agricultural ministry in Chile, tell them what we were doing and ask their permission. Also there is a gentleman based in Costa Rica, a professor there, who takes upon himself a sort of overview of Latin America in this area so we consulted him as well. We have had to go through those sorts of things in that country.

Chairman

210. If you are working in Chile with a view to the American market why did you apply United Kingdom regulations and not American ones?

(*Professor Poole*) There are two reasons for that. First of all we are a British headquartered company. We have a very strong ethical position. For agronomic reasons we have to work in areas which do not have a regulatory framework so we set ourselves the British standard. As the experiment was also going on in America we ran it through the American system as well, so we did it twice. We translated the whole lot into Spanish and walked around every single agency we could find in the Chile Government and local government and explained what we were doing. We do not want to do, and will not do, experiments in third world countries, because they have no regulations.

Lord Whaddon

211. There are a number of countries which are well known for having zero regulations. Do you not find undesirable competition or unfair competition?

(*Dr Dart*) Most of those countries are not competing with us in our market in the seeds business. In a competitive sense it is not a concern. I think in the sense of harmonising guidelines and making sure that we are all progressing in a safe way that is a concern. I know the OECD are trying to get guidelines that will apply to all the countries in their purview.

212. Is there any particular hazard you have in mind?

(*Dr Dart*) No, I am just speaking in general terms.

Chairman

213. Can you tell me whether the existence of these regulations imposes any burdens on your business strategy rather than scientifically?

(*Dr Dart*) For ourselves at the moment, no. I can see for some people it might provide the wrong sort of climate of business confidence. We are concerned, for example, by what is happening in Germany because Germany for us is a major market for most of our products. I am sure your Lordships know that there are problems in Germany with Hoechst in their insulin plant and the fact that Behringer Werke have decided to put their GCSF plant into America. That sort of thing does give us concern. Partly the regulations are affecting public perception in Germany and if that climate spreads then certainly it will affect our business developments.

Lord Flowers

214. May I ask is that peculiar to biotechnology or are there other industries you know of where people are moving to the States or elsewhere because the regulations suit them better?

(*Dr Dart*) I cannot think of any.

(*Professor Poole*) I do not really know.

Lord Perry of Walton] Animal experimentation might be the same sort of thing.

Lord Soulsby of Swaffham Prior] There is a lot of this today with animal experimentation. In fact, in Switzerland many of the major pharmaceutical companies are moving out because biotechnology involves animals, some to Germany.

Chairman

215. We have got to the stage where the Committee answers its own questions! That is very useful to all of us.

[**Chairman** *Cont*]

(*Professor Poole*) The major problem industry faces is one of confidence and trust in the attitude of the European Community and where we in Europe are going. Decisions then have to be made about where to do field trials. As I said, the Clinton administration yesterday approved their notification system. Already it costs a lot more to do the experiment in the United Kingdom than in the US so it will be even easier to do experiments in the US than in the United Kingdom. I would add on that I do not see any evidence that the US system is any riskier or any more dangerous. I think this is one of the problems we face, the belief that additional regulations, additional bureaucracy, actually increases safety. It does not, it is the appropriate level of safety regulation which guarantees it.

Lord Perry of Walton

216. Is the easing in the States due to the fact that they have a longer and bigger experience? Is this not likely to happen here as well?

(*Professor Poole*) America is one of the countries you look at as being grossly over-regulated, wherever you go you see signs telling you not to do this, or that. Do not look over this cliff in case you fall down, it is that sort of culture. In this sort of area what the Americans did, and I think we can learn from them, is first of all they had considerable public debate on biotechnology, they looked at the benefits for the American society and they looked at the risks. Then under the Bush administration they produced a number of policy papers which identified the policy. There was considerable debate, not just among the scientific community but with the legislators, the public, all sectors of society, and they agreed their policy after debate. They then put a regulatory framework in place. They have done it in such a way, because they have had special legislation, which allows them to increase or decrease the amount of regulatory oversight as experience is gained. The Clinton administration, as of yesterday, has approved the USDA policy with one minor modification which industry answered for them.

Chairman

217. On the EC Directives we were told, I think by the Health and Safety Executive, that in due course technical amendments can be made to these Directives. Are you presenting your views to the Government and possibly to Brussels with a view to influencing any changes in these Directives?

(*Dr Dart*) Yes we are, through every available channel, certainly through SAGB and certainly through our contacts with the regulators in this country. Indeed, one of the big flaws in my area in the Directives was its lack of appreciation of plant breeding and the plant breeding process and the definition of plant breeding. We had a long discussion over 14 months ago with the DoE expressing our concerns in relation to those definitions. As a result of that I think we convinced our DoE colleagues there was a problem which they have then taken to Brussels for debate there and some re-interpretation of those definitions. So it seems as if there is some re-interpretation possible within the directive but clearly the directive itself is flawed and needs re-visiting at some time in the future but we are told that is a fairly lengthy process.

Lord Perry of Walton

218. On page 6 in the paragraph you say: "Simply transferring the requirements of Directive 90/220 into vertical regulation may be an administrative solution, but we fear that this will be a case of 'building a house upon the sand'." Why? Why should that be? If they are transformed into a vertical regulation it would seem to me it could solve the problem?

(*Dr Dart*) Yes, I think we were referring to the combination of horizontal and vertical and the confusion that would create.

(*Professor Poole*) We were trying to put some feeling into the document. Just moving, for example, annex 2 of Directive 90/220 into for example the pharmaceutical legislation or into the food legislation or into the pesticide legislation is administratively nice but you are actually just transferring the problem from one regulatory track to another. You are still saying a GMO should be regulated differently, because it is a GMO. What you should be saying is: "This is a product to achieve an effect, I wish to examine the risk of that product". The fact it may be genetically manipulated as part of that investigation is not the sole driving force. I want to look at the product safety and then I bring in the fact it is genetically manipulated as part of that. Moving regulations over makes life easier but we wait to be convinced. Our legal advice, the advice of my colleagues, and experience has taught us that such a move is risky but it might be all we can do.

Lord Renwick

219. Professor Poole, it seems to me Zeneca as a commercial organisation will impose its own regulations, it will impose its own tests to make quite sure that the products that are produced are saleable and resaleable and stand the test of time and are competitive.

(*Professor Poole*) That is right.

220. What we are really talking about is are the regulations imposed either by Europe or by the United Kingdom anything really dramatically—in which section—more onerous on the company than you would impose yourselves for humanitarian and as regards the long term commercial considerations?

(*Professor Poole*) First of all, yes, we insist our review is a more strict review than anybody else can apply for us because as you said the name of my company is more important than anything. Secondly, as examples where we feel perhaps we are not prioritising our resources correctly would be Annex 2, of 220. 89 questions have to be asked and filled in. If I am examining releasing a crop plant, a wheat or maize plant in this country a lot of those questions are not relevant to the release but we still have to fill them in and explain why they are not relevant. If you wish to suggest an improvement you would take Annex 2 and say: "These are generic questions and these are questions which have to be answered for bacteria, those for a virus, those for a plant, those for animal", there is a much more

[**Lord Renwick** *Cont*]
streamlined procedure which is what we are looking for.

221. It does seem there is quite a big learning curve up which the regulators have yet to go rather like me.
(*Professor Poole*) We are all learning together.
Chairman] I am glad to hear you are going up rather than down!
Lord Renwick] Certainly recognise it is there.

Chairman

222. One of the DoE witnesses told us that the differentiation between horizontal and vertical regulations was academic, if the regulations are risk based. Do you agree with that?
(*Dr Dart*) Not at all. If I can use another example which I promised to give you earlier. We are selling a herbicide resistant corn in the States, herbicide resistant maize which is in fact resistant to a competitor's herbicide but we sell it because we believe it gives the farmer a benefit for treating some weeds. We have produced that using a traditional technique not using Recombinant DNA at all. We could have done the same experiment using Recombinant DNA. Our argument would be that in order to judge the safety of this material you look at the product. You say: "Is this herbicide resistant corn plant something that is okay in the environment and is going to be genetically stable and all those good things?" and not "Have you produced it by Recombinant DNA or have you not?" That is one of our first living real marketed examples. As it happens what we did with our product was we went to the USDA and told them what we had done for their information. We involved the local university agricultural extension services to tell them what the product was about and give them the right background and we did that in case of misinterpretation but also because this was a new product in the corn belt. It was the first product out there with this particular characteristic. That is looking at the product not looking at the way you make it.

Baroness Hilton of Eggardon

223. One of the problems it seems to me about looking at the product is that is the way you might excite public anxiety. Is this not what has happened over tomatoes in America that because you are actually looking at licensing the product people become unduly concerned about the particular product whereas in some way looking at the horizontal process may be too obscure perhaps for the public to grasp and you might not get the same sort of public panic about that particular product.
(*Professor Poole*) I think that is an interesting point, Lady Hilton. I think the answer to that is one of your own values. We wish to put a product on the market which is safe. Vertical regulation even though it is looking at products is the way we guarantee that safety. We have to live with those values, that is the best guarantee we can give of safety and that is what we are concerned with here.

224. In doing that you may in fact alarm the public more than by the horizontal process.
(*Dr Dart*) I do not understand why.

225. Because to them tomatoes are familiar or more than familiar or whatever so if you are actually looking at licensing a particular product that may grab the public's imagination whereas they are not familiar with scientific horizontal processes. You may not have a Frankenstein's monster on the ground, you are not going to alarm the public so much by just looking at that process.
(*Dr Dart*) I can understand that the public could get alarmed by somebody like Jeremy Rifkind telling them: "This is the thin end of the wedge"—

226. And holding a tomato in his hand.
(*Dr Dart*) Yes, and holding a tomato in his hand. We have to do a lot to make sure the public understand how this tomato has been created and how it relates—

227. You are looking at the processes again?
(*Dr Dart*) Yes.

Lord Flowers

228. Chairman, I am still grappling with bureaucracy, if I may.
(*Professor Poole*) Are we not all.

229. You have to answer a very large number of questions, 89, are they imposed by DoE or by Brussels and which is the harder taskmaster?
(*Professor Poole*) The 89 questions came from an OECD report in 1986 perhaps as suggestions for how to evaluate things. That report, which is actually very interesting, also made a point there was no scientific justification whatsoever for the regulation of Recombinant DNA because they are recombinant. Those questions were then taken up and put in Annex 2 of 90/220 which is a directive and which as part of Europe has to be applied in this country. Those questions, therefore, came from Brussels, not just Brussels, but from the European Community and we have to answer them under national law.

230. Who supervises your implementation of them?
(*Professor Poole*) The Department.

231. Presumably the Department?
(*Professor Poole*) Yes.

232. So the extent of the bureaucracy which you suffer, if I may use that word, is insisted upon by the DoE on behalf of Brussels?
(*Dr Dart*) To be fair to them they may say this is part of law.
Lord Flowers] What I was really going to ask next is if it emanates from Brussels then how does what DoE do to you compare to what corresponding ministers in similar countries do to their companies?

Chairman

233. I think I can add to that question by saying we are told that the Directives, the regulations and so on, are intended to provide what is nowadays called the level playing field, is the playing field level is the question?
(*Dr Dart*) Our impression is that the interpretation in other countries is somewhat different.
Chairman] I think we are running out of time, unless you are absolutely sure you must ask this question, and I am sure you are.

Lord Perry of Walton

234. Obviously ICI and Zeneca are very competent, but do you think with the growth of the subject and the money involved that new companies could spring up and pay less attention than you do to the quality of safety and if regulations are made simpler for you would they be made too simple for them?

(*Professor Poole*) The answer to that is the importance of inspection. One of the things we do support is competent inspections and we welcome that because it improves our performance and guards against the areas you were saying.

Chairman] We will have to draw to a close there. There may be further things you would like to let us have amplifying your evidence or adding to it and we would be very pleased to hear anything from you of that kind. Thank you very much.

Written Evidence from Glaxo Group Research Ltd

1. *The Glaxo interest in Biotechnology*

Glaxo is involved exclusively in the discovery, development, manufacture and marketing of prescription medicines for the treatment of human diseases. Our drug discovery and development activities are based upon the application of science and technology to understanding disease mechanisms, and from this the discovery and development of novel medicines. Biotechnology is regarded by us as essential to these activities.

Glaxo has been engaged in "biotechnology" in the form of fermentation technology for many years and this is important for our production of penicillins and cephalosporins used in the treatment of infectious diseases. Fermentation is used elsewhere in the industry in processes leading to the production of medicines such as the immunosuppressant cyclosporin, and was initially used in the discovery and isolation of the cholesterol lowering agent mevinolin. Although fermentation technology may be regarded as "old", it is still undergoing development within the pharmaceutical and chemical industries as it affords a means of using micro-organisms in the synthesis of molecules which cannot easily be made by conventional chemistry—ie by biotransformation. It should not be overlooked, therefore, in any consideration of the role of biotechnology in industry.

The more usual meaning of "biotechnology" now embraces the developments which arise out of the application of genetic engineering. It will thus cover many applications of modern molecular biology and chemistry employed in the field of gene cloning, expression of specific proteins by cells and organisms in culture, the production of transgenic animals, "gene therapy", protein biochemistry and protein structural chemistry. Glaxo does not, at present, have any proteins derived from the application of biotechnology in development as potential drug candidates. Other companies in the pharmaceutical and biotechnology industries have developed such proteins—eg erythropoeitin, interferons and interleukin-2.

Genetic engineering is used extensively throughout Glaxo Group Research for many purposes. For example, we use biotechnology as a means of providing pure proteins, such as enzymes and receptors, and modified organisms, such as yeast and bacteria, as tools in the process of drug discovery. These "tools", when applied to other disciplines such as cell biology, biochemistry and pharmacology, provide us with potential therapeutic targets and screening systems. The use of transgenic animals is being explored by us as a means of understanding disease processs and may also provide convenient animal models for human disease in which candidate compounds can be evaluated prior to entering the development process. In the case of a number of important diseases requiring new methods of treatment, animal models do not at present exist. Genetically modified organisms are also used for the resolution of racemic mixtures of compounds and the improvement of titres of natural products.

2. *How and why is Biotechnology important to UK industry?*

It is important to realise that the term "industry" covers a wide range of activities which should have the potential for wealth creation in the UK. Each sector will have its own particular problems, needs and solutions. The application of biotechnology has the potential to make a very significant contribution to the future economic success of the UK manufacturing base. Glaxo's activities are exclusively in the area of discovery, development and marketing of prescription medicines and it is only from this position we can comment upon the importance of the development and exploitation of biotechnology.

From the perspective of the UK pharmaceutical industry the understanding of the molecular basis of human diseases is essential to drug discovery research. Biotechnology is being applied to help in this understanding and the identification of target molecules at which new medicines can be aimed to provide effective specific and safe treatments. The industry in the UK has been highly successful. As evidence of this it may be pointed out that at present six of the top twenty prescription medicines in use in the world are UK discoveries. We see the application of genetics, molecular biology and biotechnology as essential for the industry if we are to be able to maintain this record of achievement.

The applications mentioned above are merely examples of the value of biotechnology in the pharmaceutical industry. They, and many other applications, will be seen to have application for other industries engaged in a wide range of activities ranging from sewage disposal to agrochemicals. Adoption of these techniques is essential if UK industry is to remain competitive and indeed UK industry should lead in the adoption of these techniques, if it is to become a world leader.

3. *What future prospects and opportunities does the technology offer?*

We believe, for reasons given above, that biotechnology has enormous potential in improving human healthcare. The human genome mapping and sequencing initiatives at present underway offer the prospect of understanding all hereditary information and understanding the genetic basis of diseases. This new knowledge will have an impact upon drug discovery in a number of ways but, in particular, will allow the identification of new points of intervention in a number of important diseases. Already we are seeing novel therapies being tested in inherited disorders, such as cystic fibrosis, and new drugs with decreased side-effect profiles. Both developments owe their existence to information provided by genetic engineering. The opportunities for reducing human suffering by exploiting developments in biotechnology to discover new medicines is now enormous.

In other areas, we can expect to see better food crops and cleaner manufacturing processes.

4. *Which developments in Biotechnology raise issues of safety and how should they be addressed?*

There is a widespread popular impression that all genetic engineering is dangerous and the products of the technology represent an environmental and/or health risk. This is clearly wrong. Legislation on safety which panders to this view is not useful and is likely to be ignored by many who see it as illogical.

'Genetic engineering' has gone on for centuries in the form of selective breeding programmes and many of the domestic animals and food crops we have today are products of this. Nonetheless, the new technology does offer the opportunity to mix the DNA from species which could never have been mixed by traditional techniques. Thus, it is not difficult to see that toxin genes could be introduced into normal human commensals such as *E.coli*. Clearly such organisms would be dangerous and should not be made without adequate containment and other precautions.

Most of the safety issues surrounding biotechnology, such as deliberate release and contained use, have been covered by existing legislation but the situation is not entirely satisfactory. We believe that there is too little interpretation of EC Directives so that they fit with the local situation and there is, rather, the desire to alter the local situation so that they fit with the letter of the EC Directives. It must also be noted that anyone deliberately setting out to make a dangerous organism, for any reason other than legitimate research, might not feel constrained by existing legislation. The current legislation thus runs the risk that it could unduly restrict legitimate and largely safe experimental work whilst making no provision for dealing with those who set out to mis-use the technology.

The ethical considerations of those aspects of genetics relevant to our industry and human medicine and their implications, particularly with regard to the rapidly developing use of gene therapy, are adequately addressed by the Clothier Report.

A further consideration of importance in the context of legislation and regulation is the likely effect upon industrial competitiveness. We suggest that an excessive bureaucracy in this, and other fields, will have a detrimental effect on competitiveness.

5. *Should Biotechnology be regulated by an industry-specific regime?*

We believe that there is every reason for industry to be encouraged to regulate itself in respect of its use of biotechnology, and of the products thereof, rather than be dictated to. We do not consider that there is any good reason why biotechnology should be regulated in an industry-specific manner because biotechnology research in industry uses precisely the same techniques as biotechnology research within academia and should thus be regulated in the same way.

Legal requirements of the Health and Safety at Work legislation impose responsibilities which are such that industrial organisations must be responsible for the safety of their own staff and environment. Over the years that such regulatory requirements have been in force, industry has gained considerable knowledge of the safety issues in question.

The quality of biotechnology products in the pharmaceutical field are, like other medicinal products, subject to regulatory control by means of guidelines such as the "Notice for Applicants" and the requirements imposed by directives for "Good Laboratory Practice (GLP)", "Good Clinical Practice (GCP)" and "Good Manufacturing Practice (GMP)".

These safety and regulatory requirements adequately cover any differences between industry and academia.

6. *Where products are concerned is horizontal regulation better than vertical regulation?*

Horizontal regulation implies the judgement of the safety of a product through the process involved in its production whilst vertical regulation is concerned with the characteristics of the product itself.

In the pharmaceutical industry our products are regulated in a manner that does not recognise these two distinct modes. Thus the characteristics of the product with regard to both safety in use and clinical efficacy are addressed, but in addition the production process is also subjected to auditing and regulatory control through such directives as those regulating GLP, which is relevant to the development stage of an entity and GMP. The predevelopment phases of drug discovery research are not regulated by GLP and any attempt to introduce such regulation at this stage will have a serious and detrimental effect upon the creative processes involved in successful drug discovery.

As far as Glaxo is concerned, we do not have any products originating directly from biotechnology. This is likely to be true also for many other companies in the industry. Our use of biotechnology is, as has been outlined above, as a provider of "tools" and is concerned with the discovery of novel medicines. The final products emerging from these activities will usually be molecules derived ultimately from medicinal chemistry. We thus believe that there should be little horizontal regulation of the process because, if it were applied in our context, it would involve probing in areas of little direct concern to the final product and such regulation would be counterproductive. For example, if carried to an extreme, the development of drug discovery screens would be covered although they will be of no relevance to the final product's characteristics.

We believe that ultimately it is, in general, the characteristics of the compound itself which are more important than the processes by which it is derived. They are however clearly related, for example the process of production is relevant *vis-a-vis* expected or potential contaminants, but the current regulatory requirements address both issues adequately. During the process of product approval products derived by the use of biotechnology are subject to guidelines over and above those now applied to new medicines. Further regulation should be resisted unless such measures are clearly required.

7. *Should regulation evolve from a horizontal to a vertical approach in each industrial or environmental application?*

We believe that it should for reasons already stated above.

8. *How do current Regulations compare with those of other competitor countries?*

In Europe the regulatory climate is very variable between countries, even within the EC. The EC Directive in this area has unfortunately not yet been given effect by legislation in all EC member countries. Furthermore, there is considerable variation in the interpretation of this legislation throughout Europe. For example the interpretation has been very strict in countries such as Germany and Denmark, but as yet in Italy there is an absence of legislation as yet.

In the United Kingdom "The Genetically Modified Organisms (Contained Use) Regulations 1992" and "The Genetically Modified Organisms (Deliberate Release) Regulations 1992" were created in response to the EC Directive. We believe that in general the UK has adopted a more sensible approach to the issues than many other countries in Europe but there is evidence of a less than consistent attitude between Government Departments and Agencies. For example the HSE appears to have adapted a good intermediate position whilst the Department of the Environment appears to be far more rigid and less helpful.

The situation in the United States of America is much less bureaucratic and more enlightened. The starting position arises from the general assumption that most genetic engineering results in benign organisms rather than the assumption that genetic engineering is dangerous and should be minimised. Experience over the last twenty years has does not support this general position as there has been a lack of incidents involving genetically modified organisms during this period.

We have no knowlege of the situation in Japan and the Far East. However, it is our expectation that Japan would follow the lead of the USA.

We suggest that the key to sensible and successful regulation in the field of biotechnology lies in Governments taking advice from experts, drawn from both industry and academia, with the right knowledge and experience of relevant areas of science when formulating polices in this area.

9. *What are the consequences, or likely consequences, of the regulatory regime on competitiveness of UK industry?*

The pharmaceutical market is a global market and to remain competitive the industry must seek to carry out its drug discovery and development activities in those environments which are most encouraging and amenable to progress in a rapidly evolving area. Thus excessive regulation will be detrimental to all aspects of our business from the research activities to the market. If regulatory measures in any country place unreasonable restrictions on this work the result will inevitably be a transfer of activities to more sympathetic regimes.

10. *Is there a danger that the present regulatory regime will prevent the exploitation by British industry of research conducted in the UK Science Base?*

We are assuming that the term "Science Base" in the question refers to those scientific and technological activities that take place within public sector institutions such as the Higher Education Institutions (HEIs) and Research Institutes. It is our view that there is not this danger at the present time, however there is a risk of this happening in the future. We are more concerned at the present time however with the serious decline in the HEIs and Research Industries and the possibility that there may be no UK public sector science base for UK industry to exploit.

11. *How best can issues of public acceptance be addressed?*

There is considerable ignorance about genetic engineering in both the public and the media. There is a tendency for the media to pick up and emphasise the negative aspects of biotechnology, that is the risks, rather than referring to the benefits that have already accrued from the technology and the potential benefits for the future.

It must however be admitted, that scientists working in the field are reluctant to explain their work in ways which are easily understood. This tendency creates an atmosphere of suspicion in the mind of the public and this can translate into antagonism. Biotechnology must be projected as a positive contribution to the health and welfare of society and issues of concern openly discussed. More contact between researchers and the media and public should thus be encouraged. An improvement in the quality of scientific journalism would be a major advance.

12. *What other factors do you consider will play a crucial role in the competitiveness of the UK Biotechnology industry?*

We believe that it is essential that the public sector science base in the UK is adequately supported in order that biotechnology, and other important areas of biological and chemical sciences are advanced in the UK. A healthy science base must be regarded as essential for the long term competitiveness of UK industry.

The UK Biotechnology industry, which could be a major contributor to our industry, requires better financial support than it is at present experiencing. The industry is at a disadvantage when compared with the better developed biotechnology industry in the USA. In the UK the venture capital view of biotechnology is short term and this situation is not helped by the British taxation situation and the UK Stock Market Rules. The result of this is that much good British academic science is not being exploited or, as has happened, is being exploited in other countries and in particular in the USA where UK academics find a more sympathetic reception for their inventions and ideas.

SUMMARY

1. Biotechnology in the form of fermentation technology has been widely used by Glaxo and other pharmaceutical companies for many years for the production of antibiotics and other important medicines. The "new biotechnology", which includes genetic engineering, offers considerable potential for the elucidation of the molecular basis of human diseases and the identification of novel targets for therapeutic intervention. It is regarded by Glaxo as a most important enabling technology for the discovery of molecules that may form the basis of new medicines for human diseases. We do not at present use biotechnology as means for the direct production of proteins and peptides as new therapeutic agents or vaccines although other companies in the biotechnology and pharmaceutical industries do.

2. Whilst it is important that we recognise the potential risks of biotechnology and the public sensitivities which surround the subject, it is important that the field does not become so regulated that progress is severely hampered or becomes impossible.

3. We believe that the current situation regarding regulation in the UK which has arisen in response to the requirements of the EC directive are broadly acceptable and will not seriously jeopardise the development and use of biotechnology in our industry. This is in contrast to the situation in other member States of the EC in which regulation is stringent and inhibitory or, at the other extreme, too lax. The USA, a major competitor in the biotechnology field, has a more enlightened view of regulation and is less bureaucratic than European regulations.

4. We believe that excessive regulation will be detrimental to our business and will reduce the competitiveness of UK industry.

5. The public perception of biotechnology, encouraged by the media, is a generally negative one and this does need to be changed. There is a need for scientists working in the biotechnology field to become more ready and open to discussing issues raised by the subject in the public mind.

6. Regulation is not the only threat to a healthy UK biotechnology development. Attention is also needed in the area of provision of financial resource for biotechnological innovation. In particular there needs to be a longer term view of the subject by venture capitalists, an encouraging taxation regime and a change in the Stock Market rules.

Examination of witnesses

Dr J B Ward, Director of Microbiology and Dr M Weir, Head of Protein Biochemistry, called in and examined.

Chairman

235. Good morning. Thank you very much for coming to continue our education in this matter. I wonder if you would introduce yourself and your colleagues and if you wish to make a short statement on your general position in relation to biotechnology?

(*Dr Ward*) Certainly. I am Barrie Ward, I am the Director of Microbiology for Glaxo Group Research and I am accompanied today by Dr Malcolm Weir who is Head of our Protein Biochemistry Department. As you know Glaxo is one of the world's major pharmaceutical companies. We approach biotechnology in the sense of using it as an enabling technology. You are probably aware that we do not market biopharmaceuticals at the present time although clearly we do not eliminate this from future work of the company. As I said, we see biotechnology as an enabling technology which allows us to work in the discovery of new drugs. It provides a mechanism for us to obtain pure proteins, enzymes and receptors, particularly modified organisms as tools in drug discovery. Now we are starting to develop transgenic animals as potential models of human disease that will allow us to screen compounds more rapidly without actually having to go forward to man. I do not think we should underestimate our involvement in improving strains of micro-organisms for the production of natural products. Glaxo is one of the pioneers in terms of fermentation, old-style biotechnology. Whereas biotechnology in the public mind today has come to mean genetic manipulation and genetic engineering. I think also we should not forget the potential use of genetically modified organisms in the production of chiral compounds from racemic mixtures, that is the separation of mixtures of a compound that may be synthesized where one batch of that mixture's particular chemical structure carries with it the potential benefits and hopefully not the associated toxicities and in many instances enzymes can be used to separate those mixtures where chemistry would be extremely difficult. We have practice inhouse doing that and we use, or intend to use, genetically manipulated organisms where they provide benefit in terms of higher yeilds of specific enzymes, for example. Thus our underlying philosophy is as an enabling technology, but we do not rule out moving in the future into areas that we might define as biopharmaceutical.

(*Dr Weir*) I would like to underline the central nature of biotechnology for a great deal of the work we do now in the pharmaceutical industry and it should not be seen as a separate entity. 20 years ago there was no biotechnology, apart from fermentation technology going on in the pharmaceutical industry but now I think most of the techniques that form that technology are central to what we do in drug discovery from the identification of targets for therapeutic intervention through to the discovery of compounds and further developing of those compounds to get them into the clinic as medicines for major diseases. It is crucial to take that on board because it is essential technology and without it a modern pharmaceutical company could not survive.

236. As far as drugs are concerned, can you see a day coming when chemically produced drugs are largely replaced by biotechnologically produced drugs?

(*Dr Ward*) I think the simple answer is no. I see biotechnology and biopharmaceuticals as complementing the work of chemical drugs in the sense that there will clearly be some areas where biopharmaceuticals will be of benefit. Gene therapy may be a case in point where particular genes are constructed and then given to patients with a particular disease. I think there are many instances where it will complement but I cannot see in the future, at present, where they will actually replace.

237. But it might take quite a bit of the market, do you think?

(*Dr Ward*) I think it will take some of the market. When one defines "quite a bit", I think we are used to seeing in the press very large numbers quoted against biopharmaceuticals and I think with some of these we have to be very careful that those numbers have not been inflated because of reasons other rather than the actual market potential.

(*Dr Weir*) You have to think of it more in terms of creating new markets because new possibilities will arise which could not be addressed by the previous technologies. It will not be so much that you will replace aspirin with a protein, it is more a case of tackling some areas such as cancer or vaccine development where there is no good chemical way of tackling those problems and biopharmaceuticals, proteins, genes or whatever packaged in whatever way will enable us to treat diseases we could not otherwise treat. There will still be a great effort on making small molecule chemicals that interdict in biological processes because they have very good properties in terms of their synthesis and their transport into the body. The delivery basically is pills. There is a lot to be said for small molecules in terms of control of treatments.

[**Chairman** *Cont*]

238. Could you tell me is there any difference between natural insulin and GMO derived insulin?

(*Dr Weir*) The two different forms of insulin have actually been studied by x-ray crystallography which elucidates the atomic structure to a high resolution and there is no difference in those studies of the atomic structure of the insulin concerned. There is a difference in the initial use and treatment. There were some differences in how the diabetic patients responded to the different treatments and those have since, as I understand it, been put down to the greater levels of purity of recombinant insulin over the natural porcine-derived insulin and it is the change in the pharmaceutical regime. You get similar things happening when you switch to different types of drugs that act in the same way in traditional medicine.

239. So you are saying there is no scientific difference though there might be a difference in purity?

(*Dr Weir*) I think there is a scientific difference in that regard. There are two different questions. Are the molecules the same? And the second is are there other molecules in there the same or different? I do not have a deep understanding of this. Insulin is not anything we have been working on in Glaxo but, as I understand it, the difference is in the contaminants rather than any other problem to do with the insulin molecules.

Lord Perry of Walton

240. The molecules are different in purity.

(*Dr Weir*) In terms of the overall fold of the protein.

241. They are two different substances.

(*Dr Weir*) In that regard they are different, yes.

Chairman] Back again to answering your other question.

Lord Perry of Walton] I am sorry.

Chairman

242. No, no it is good I think. Let us think a bit about the regulatory system under which you work. Do the United Kingdom regulations affect your competitiveness as a company for good or ill?

(*Dr Ward*) I think at the present time the answer to that is that they do not but I think within the company there is concern that depending upon their interpretation then there is the possibility that they could affect our competitiveness.

243. But they have not so far?

(*Dr Ward*) They have not so far but we are in a situation where we do not yet know quite know how these new regulations are going to be interpreted.

244. Now to a large extent these regulations are for the protection of the public and so on. What risks do you see in biotechnology and do you think the regulations are effective in dealing with these risks?

(*Dr Ward*) I think we have to recognise that within biotechnology then there have to be a multiplicity of risks depending upon the system with which you are working. I think one of the problems that we have at present is the perception that just because it is genetic manipulation it provides an overall risk that requires very strict regulation. I think we have got to step back from that. Clearly if we were working with potential toxins or producing very pathogenic bacteria or viruses then we would need to adopt a certain regime for the use of this whereas in other cases, perhaps we were looking at a receptor or an enzyme that is fairly ubiquitous among mammalian species or even among bacterial species then the risk associated with work of that type I believe would be less. We are coming from a premise that all genetic manipulation is evil, if can put it that way, or has a very strong risk associated with it. I think I would prefer to argue that there are risks associated with it but we need to take this on a case by case basis. We have a long history in this country of very effective regulation of genetic manipulation which I think we should recognise.

245. Do you think it is satisfactory from the point of view of protecting the public?

(*Dr Ward*) I think there are a number of issues here. We must distinguish between laboratory research, which is really what we do now within Glaxo, through let us say drug development to commercialisation and at each stage risks will need to be assessed but in terms of laboratory research I think the way the Advisory Committee regulations have been handled in this country have been really very very successful and I do not think we should lose sight of that.

Lord Perry of Walton

246. All you are doing at the moment is in a contained sense. You are not marketing.

(*Dr Ward*) We are not marketing.

247. You are marketing pure chemicals.

(*Dr Ward*) We are marketing pure chemicals.

248. Am I right in thinking after doing your drug screening on the isolated receptors, GMOs, whatever it may be, that you make the new compound without any contact with the GMO at all? It presumably then becomes a scientific process which has nothing to do with the GMO at all?

(*Dr Weir*) Our whole business is geared around using GMOs and the way we use them has a great effect on what we do.

249. That is in the research field and development field but in the manufacturing field you move away from that?

(*Dr Ward*) There was a time, you are quite right, when Glaxo was involved in the vaccine business but that was at a time when genetic manipulation had not come into play. We have never been involved in that way.

250. What I am trying to get at if you find a new drug with your screening using GMOs it may be they have been manufactured in a wholly separate building where there is no GMO contact whatsoever in which case you are not, in my view, falling within the release side at all.

(*Dr Ward*) We are not falling within the release side; we are only working within the contained use side.

(*Dr Weir*) That is our understanding of the legislation. That is an issue of interpretation. That is how we interpret the EC Directive and GMO regulations on contained use and deliberate release.

Lord Soulsby of Swaffham Prior

251. Presumably, Lord Chairman, the fact that you are using this as an enabling technology means that you come under less criticism than you might do if you were producing genetically modified vaccines or organisms.

(*Dr Ward*) I think that is true at the present time. Within Glaxo there is certainly a degree of uncertainty as to how the contained use regulations are going to be interpreted. I guess that is what I am trying to get across to the Committee.

Chairman

252. Does that mean that the degree of uncertainty about the regulations determines to some extent your business strategy?

(*Dr Ward*) No, it has had no effect on our business strategy to date.

253. At all?

(*Dr Ward*) To date but clearly the interpretation of the regulations might. I think we have seen this within Europe where there has been a different degree of interpretation and the effect that has had on strategic decisions within other areas of the pharmaceutical industry. I think we have to recognise that we are working in a global industry and that in certain countries, for example, Germany—which I am sure we are all aware of—there the impact of regulations and the impact of pressure groups has caused a significant withdrawal from work of this kind.

254. Can you give us some examples of this?

(*Dr Ward*) The Hoechst insulin plant in Germany has never actually operated.

255. Are there others?

(*Dr Ward*) I believe there are others. In terms of information that we have heard with regard to other production pharmaceutical companies they have not developed there in the way that one might expect them to do.

256. Germany is particularly sensitive?

(*Dr Ward*) Germany is a particularly sensitive country, yes.

Lord Perry of Walton

257. I take it from the regulations there are two kinds of process in dealing with the laboratory side; one is getting consent in advance and the other is notification?

(*Dr Ward*) Yes.

258. Is a problem in dealing with isolated receptors and things of this sort the fact you worry about having to get consent? If you simply notified there would be no problem?

(*Dr Ward*) I think that is correct. In the past, as you are aware, in the Advisory Committee guidelines on genetic manipulation it was clear that we could take a certain view in-house and notify the HSE of the view that we had taken. Now we appear to be in a situation where we are going to have to seek consent before we can actually carry out the work.

Lord Whaddon

259. Some countries are notable for not imposing regulations—Italy has had a very relaxed view on medical regulations for as far back as one can think. Are you aware of any difficulties that are arising in Italy in this work due to a lack of regulation?

(*Dr Weir*) You mean instances of accidents or anything like that.

260. Yes, first of all. Secondly, do they gain any advantage over you for that which you have regulations and they do not?

(*Dr Weir*) I am not aware of any accidents that have occurred.

(*Dr Weir*) Not to my knowledge.

(*Dr Ward*) In terms of advantage I think again that is very very difficult to judge. Much of this work is not carried out in the public domain, so it is difficult to know what advantage they have got or not at the present time. I do not think we can answer the question.

261. Would you rather that they were regulated?

(*Dr Ward*) I would be much happier, to use the colloquial phrase, to see a level playing field.

Lord Renwick

262. We have heard before about levels of inspection. Obviously in the United Kingdom there are relevant levels of inspection, but do you think there are in other European countries, following on Lord Whaddon's question?

(*Dr Ward*) I can only comment in terms of our own operations which are in Switzerland and in Italy. As far as I am aware, there is no inspection in Italy. I have never heard any comment about any inspection having taken place there. The amount of genetic manipulation that we do in our laboratories is relatively small. In terms of the Glaxo Institute for Molecular Biology in Geneva, then I believe that they are inspected. They are certainly expected to work to the same standards that we work to within Glaxo.

263. Would you like to speculate on what risks might occur on totally uninspected activities if there were any cowboys in your profession, God forbid?

(*Dr Ward*) I see no reason to believe why our profession is any different from anybody else's. I am sure there are cowboys. Perhaps this is not the answer you are seeking, but I think if I can turn it round the other way and say, if the regulations and the inspection criteria are onerous then this puts a greater emphasis on cowboys perhaps taking the chance and doing things outside those regulations if they believe that they can get away with it.

264. For a short-term advantage only, because unless they impose their own strict regulations they might possibly produce an image-damaging product?

(*Dr Ward*) I think that is right. I think it is a balance, is it not? If they do not produce an image-damaging product then, in effect, they have got away with it.

Chairman

265. Did you say you have an operation in Italy?

(*Dr Ward*) Yes, we do.

266. Is it inspected?

[**Chairman** *Cont*]

(*Dr Ward*) Not as far as I am aware.

267. Is that the reason why it is in Italy?

(*Dr Ward*) No, it is not. I did point out the amount of genetic manipulation work we actually do there is very, very small.

268. We have heard quite a lot in the few weeks we have been undertaking this investigation about horizontal and vertical regulations. Have you any views on these? The DoE told us the difference between them was academic but others have told us that it is not. What do you think?

(*Dr Weir*) I think the key issue for regulation of a product is what actually ends up in the product. If, as is the case in traditional medicines, those regulations take into account how the product is made then that is sufficient in terms of regulation; because you can make a connection if you think a process may lead to some contaminant. For example, if you made a blood product from blood sourced in different countries that were prone to different transmittable diseases that may be blood-borne then you would consider those differently because of where they came from. In an ideal world you should be able to measure everything that is in the pot anyway, and you would not have to worry about those sorts of issues, but in practice they should be taken into account. I see no reason to regulate separately the process from the product. The processes are regulated. We have to do things in industry to good manufacturing practice, good microbiological practice, good laboratory practice, and to get products on the market we have to follow those rules. In essence I think that vertical regulation, as I understand it, would subsume horizontal regulation if it was done properly.

(*Dr Ward*) I think we have to clarify that we are talking here only in terms of medicines and biopharmaceuticals.

Lord Soulsby of Swaffham Prior

269. I am interested in your comment about good laboratory practice and the rest. While I accept what you say in terms of control and inspection should be sufficient, there have been one or two major compounds that have come out medicinal compounds that have got on to the market without these. They were not following the guidelines at all, and in fact were breaking the guidelines. This is in the United States, not mentioning the firms of course.

(*Dr Weir*) That would be a very serious thing, but I think with any guidelines or rules that you have that could happen if they were not properly prosecuted.

270. What is the safeguard now? I think the public are a lot more concerned about genetic modification and the gene. They perceive perhaps, quite wrongly, that these may do infinite harm. While the testing of a pharmaceutical product can be fraudulent, the public perceive that fraudulence in the genetic side is of much greater seriousness than just the chemical side.

(*Dr Weir*) I would see no grounds for that perception. I really would not. I think that at the end of the day if you are producing a protein therapeutic by recombinant means then you have a set of problems which are specific to that particular product and they need to be considered in that way.

271. In your case, yes, you are using this as an enabling technology, which is not always the case with biotechnology?

(*Dr Ward*) No, but I think with, say, a protein that is developed by genetic manipulation that people wish to market, if the same regulations apply that are currently applied to any other drug substance with the same rigour then I think the public is safeguarded. I accept what you say in terms of the current public perception in terms of genetic manipulation, and I think that is something we probably will address later on in terms of how this might be improved or how it might be manipulated. In a sense, I think we have to refer back to Lord Renwick's previous comments, in the sense that you can make the most rigid regulations but if people perceive that there is a major benefit to be obtained by ignoring them they will ignore them until they are caught. I think it is very, very difficult to legislate for those sorts of situations. I think, thank God, that they are relatively few and, of course, whenever they do happen that they achieve maximum publicity.

Chairman

272. Can you tell me, have you much experience of dealing with the regulations in the United States?

(*Dr Ward*) Yes. Malcolm in fact has spoken to our people in the Glaxo Research Institute prior to our coming here.

273. Is it an easier world there or more rigorous? Is it easier to deal with and less bureaucratic, for example?

(*Dr Weir*) Yes. As I understand it from discussions with the biological safety chairman in the Glaxo Research Institute, the amounts of paperwork involved, in growing, say, at a ten or 20 litre scale a recombinant organism, are negligible compared with what we have to do. It is much easier and there is a blanket cover and inspection of the site. There are National Institutes of Health guidelines which are voluntarily followed in the United States. The difference is mainly one of degree, I think. It is not a case that they are not regulated, they certainly are, and they do understand there are risks inherent in these processes, as is the case in any manipulation of a bio-active substance or a biological agent.

274. Do you think the United States' regulations give a similar degree of protection to what we have in this country?

(*Dr Weir*) That is my perception from discussions; it is not from firsthand experience.

275. Would you like to see the United States system applied here?

(*Dr Weir*) Yes, I would.

276. You would.

(*Dr Weir*) Yes, I think it would cut down our paperwork. It would not, in my opinion, entail any greater risk to either the public or to the health of my staff who have to do the work.

Chairman] One of the things I like about these two witnesses is they use words like yes and no at appropriate times!

Lord Renwick

277. May I ask, Dr Weir, what would be involved in making the change from US regulatory procedures to United Kingdom regulatory procedures?

(*Dr Weir*) I have mulled this over when I got the questions sent to me. I think one way of simplifying things and streamlining the regulations would be if we considered the handling of Genetically Manipulated Organisms in the same way we consider other health and safety issues and other environmental issues in the company, in other words if the GMO regulations were part of the ACD category, that is the Biological Agents Directive, part of COSHH I see no *prima facie* case for having separate regulations for GMOs. If we consider, for example, a process that does not involve any genetic manipulation, we consider the safety aspects component, aspects of the health of the public and the health of the people doing the work. These are major issues on concern to us.

Chairman

278. I wonder if I could ask you to let us have a brief paper comparing the United States and United Kingdom regulations?

(*Dr Weir*) Certainly.

Chairman] Giving your opinions on them by the way.

Lord Renwick

279. Before we leave this subject could I ask you whether you have put this to health and safety organisations and others and what was their response?

(*Dr Weir*) I have not actually put it to them because the recent EC Directive implementation has only just come through. One lives with regulations and I would not criticise the ACGM regulations unduly. We have got used to them. We know the system and we have only had to do retrospective notification. There has not been this issue of prior permissions to do work. It is still unclear to me and many of my colleagues to what extent the EC Directive and its implementation will actually affect in practice the work we do. I think there are many ambiguities surrounding it. We have not got clear yes and no messages from these documents because they are meant to be interpreted. I think it is common practice that will tell us whether these regulations are onerous or not.

Lord Whaddon

280. You have spoken very intelligently about the regulation of hazards. Do you take the view that there are any ethical problems in biotechnology, for instance with transgenic animals and chimaeras? If there are such problems how do you deal with them?

(*Dr Weir*) I think there are clearly ethical problems when it comes to genetic manipulation in human beings. These are massive ethical problems. Those are addressed in the Clothier report and really quite well addressed in that report. In terms of transgenic animals there are always ethical problems in these types of manipulation whenever one does work with animals. There are ethical considerations but again animal breeding and the selection of different traits in animals basically via environmental pressure on the genetic make up of those animals is a time-honoured thing to do and I would not necessarily see those ethical problems as being insurmountable.

281. But the present regulations do not deal with that, do they?

(*Dr Weir*) I think the animal regulations do because the prime consideration in the ethics of the experiments you are doing and the suffering it causes to the animal, is whether that suffering is justified, if there is any suffering, by the experiments you are proposing? They are very strictly regulated and properly regulated by the Home Office.

(*Dr Ward*) I certainly support Malcolm in that. The way the Home Office regulations in terms of animal experimentation are conducted in this country are to a very very high standard and we have frequent dealings with the Home Office Inspectorate and the issues are addressed with them as we proceed.

282. Yes, I agree but this of course is not an EC regulation?

(*Dr Ward*) No, it is not, that is right.

Lord Perry of Walton

283. You say in paragraph 11, "Biotechnology must be projected as a positive contribution to the health and welfare of society and issues of concern openly discussed." I agree wholly. Do you consider it is the responsibility of the industry to permit this and pay for it or do you think it is purely a matter for government?

(*Dr Ward*) No, I think this has to be a partnership—I really do believe that. I think it is one of the major issues that we have to address in this country at the present time. Since we are specifically talking about the United Kingdom—although it clearly happens in other countries as well; it is an international issue—I believe that science in this country is incredibly badly reported. I was thinking a lot about this last night but I think on reflection it is no worse reported than any of the other news! The whole premise on which we work today is—again to use a colloquial term—in terms of the "sound bite". If it is negative it is good because you can get a message over immediately and the whole way the public is fed information today is done in that way and so science is really no different. I think we have specific issues here that we should address and we can address and I think that industry should certainly play a part in this. I think government also has a role and that initially the targeting should be at the level of schools. The battleground is in the classroom. I do not think there is any doubt about that and the potential impact of biotechnology in terms of the health of the nation and the productivity of the nation needs to be got across to these people. We have less of a problem in terms of medicine than obviously they do in other areas but it is still trivialised. The whole reporting of it is trivialised. I think if only we could do something in terms of getting it across that scientists are serious about what we are doing and do think about the impact of our work; we would all benefit.

284. It costs a great deal of money to reach the general public in a general way the profits of

[Lord Perry of Walton *Cont*]
biotechnology are going to go to the industry rather than to the government.

(*Dr Ward*) With respect, I do not think it takes a great deal of money to get to the children in the classrooms. I think we could do a significant amount of work there for a relatively small amount of money.

Chairman

285. You mean the industry would do the work, do you?

(*Dr Ward*) I think industry is starting to do some work, yes. If we revert back to Lord Whaddon's comments in terms of animals, I think ABPI has done significant good work in terms of getting the risks of animal experimentation across to teachers and to children. They may not have been very effective yet but they are actually trying to do this. I think we need to so similar things in terms of biotechnology.

286. I think we have probably come to the end of our questions. Is there anything you would like to add at this point which we perhaps have not touched on which is of interest to you?

(*Dr Ward*) I think we have covered most of the things. I would make one final point, I think, that without doubt we, within Glaxo, see biotechnology as a vital sector as far as the United Kingdom is concerned. I think we must address the issues somehow, whether it is industry and government together, which I think is the way we should move forward; we must address the issues of being able to build on our traditional strengths of supporting the science base within the country in this particular area, and in improving the public perception, not only in biotechnology but of science as a whole.

(*Dr Weir*) I would echo that. I think the reason why we have a strong pharmaceutical and biotechnology sector here, relative to, say, other parts of Europe, is that we have a good traditional strength in molecular biology and structural biology. That is a critical strategic area in the country to maintain.

Lord Perry of Walton] That is the responsibility of government.

Chairman] I do not think we want to go into that at the moment, although we may later when we come to our report. Thank you very much for coming. If, when you receive a transcript of the evidence, you feel you want to amplify any points or add to it, we would be very pleased to hear from you. Thank you very much.

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HOUSE OF LORDS SESSION 1992-93

MINUTES OF EVIDENCE
TAKEN BEFORE

THE SELECT COMMITTEE ON SCIENCE AND TECHNOLOGY

(SUB-COMMITTEE II REGULATION OF THE UK BIOTECHNOLOGY INDUSTRY AND GLOBAL COMPETITIVENESS)

Thursday 15 April 1993

CELLTECH LIMITED
Dr J R Birch and Dr G Yarranton

BRITISH BIOTECHNOLOGY GROUP plc
Dr K G McCullagh and Dr N R Scott-Ram

AGRICULTURAL GENETICS COMPANY LIMITED
Professor P Boseley and Dr R H Gilmour

ANIMAL BIOTECHNOLOGY
Professor C Polge and Mr A Talbot

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THURSDAY 15 APRIL 1993

Present:

Flowers, L.	Renwick, L.
Hilton of Eggardon, B.	Soulsby of Swaffham Prior, L.
Howie of Troon, L. (Chairman)	Wade of Chorlton, L.
Platt of Writtle, B.	Walton, L.

Memoranda by Celltech Ltd and British Bio-Technology Group plc are printed separately

Examination of witnesses

Dr J R Birch, Director of Development and Dr G Yarranton, Deputy Director of Research, Celltech Ltd; and Dr K G McCullagh, Chief Executive Officer and Dr N R Scott-Ram, Manager, Executive Office, British Bio-technology Group plc, called in and examined.

Chairman

287. Good morning, gentlemen, and welcome to the Committee. I wonder if you would care to introduce yourselves and let us know a little about what each of the two companies does and your attitude towards the enquiry?

(*Dr Yarranton*) My name is Dr Geoff Yarranton, and I am Deputy Director of Research at Celltech. Celltech was Britain's first biotechnology company. It is divided into two halves, a contract manufacturing business for the contract manufacture of monoclonal antibodies, and Dr Birch will talk more about that. It also has half of the company involved in research for the identification of novel therapeutics, both proteins and low molecular weight chemical entities. We have been in existence for around 12 years and were founded and based on using monoclonal antibody technology and also recombinant DNA technology, that is using the technology we will talk about today and the regulations associated with it. This technology the basis of our research activities and is very important to our research activities both in terms of the scaling up and production of therapeutic proteins, particularly monoclonal antibodies from genetically engineered mammalian cells. We also use both microbial systems and mammalian cells for the production of reagents for our research activities and for our own products, hence the regulations under discussion are very important to us. Any changes in those regulations obviously have an impact on our capability to carry out those research activities and the manufacturing activities.

(*Dr Birch*) I am John Birch. I am Director of Development at Celltech in that part of the company which provides contract services to the pharmaceutical industry and to other biotechnology companies. Since the company was founded we have become very expert in producing recombinant proteins and monoclonal antibodies, particularly by the culture of mammalian cells. We provide a contract manufacturing service to make those proteins and those monoclonal antibodies to companies around the world, and in fact we are now the world's largest contract manufacturer of those proteins. I think that, in a nutshell, tells you what that part of Celltech does, and Dr Yarranton has already indicated why we are interested in these regulations and an opportunity to discuss them.

(*Dr McCullagh*) I am Keith McCullagh, the Chief Executive of British Bio-technology Group plc. British Bio-technology is currently the only biotechnology company listed on the London Stock Exchange and, indeed, is the only publicly listed company in Europe in biotechnology. I am here this morning with Dr Nick Scott-Ram, who is an Executive Manager in the Corporate Office and, prior to joining British Bio-technology, was Chief Executive of Oxford Virology, another biotechnology business. He has substantial experience of the impact of new processes and biotechnology regulations on the industry. Let me say a few words about British Bio-technology and then something about our attitude to regulations in general and more specifically to regulations in biotechnology. British Bio-technology was founded in 1986; we are therefore seven years old at the moment and we employ about 300 people. We are building a company which we expect and anticipate will be a major new international corporation in pharmaceuticals. The company will sell and market pharmaceuticals worldwide. Those pharmaceuticals will be based on innovation and new technology applied to human health care. To give you some examples of the impact that that can have, let me just mention that the current products we have in clinical trial include a therapeutic vaccine for the treatment of people with HIV infection, which is currently in multinational clinical trials throughout Europe, in phase II testing as it is known technically. Later this year similar trials will start in the USA funded and managed by the National Institutes of Health. This vaccine is a very sophisticated biotechnology-derived product, a product of yeast fermentation, a virus mimic that is totally inert and cannot cause disease but boosts the body's own immune system in order to improve the body's capacity to keep the virus of HIV latent, and therefore protect individuals with HIV and prevent them getting the disease. We have another product being developed with Glaxo, a new anti-asthma drug with which Glaxo will conduct international phase II clincial studies towards the end of this year or early next. We have sepsis trials going on in Liverpool and in Scotland with a new anti-sepsis drug. We also have a anti-pancreatitis product under development. This gives you some feel for the scope, I think, of what we are doing. We are building an international business based on new product flow from R&D. None of those products have yet reached

[Chairman *contd.*]

the market. Our first product will probably come into the market in 1996, so we are about three years away. They are all strongly patented. The company is owned primarily by United Kingdom institutions, although it is fair to say that British Bio-technology has an international spread of investors, including Japanese and American institutional investors; but the majority of our shares are owned by the top 40 to 50 United Kingdom institutions. I go through that because I want you to understand that biotechnology has the power and the capacity to build a new industrial sector for Britain and for Europe. If we are successful I hope we will be pioneering a route to company success that will generate wealth and employment for the people of Britain. How then do we approach regulations that impact the biotechnology which we are using? I think wherever you are building something that is intended to be successful you should pay attention to quality. That is no different in the pharmaceutical industry. We firmly believe that one should have standards of high quality and professional integrity in their application and that we should take care to protect the people who work for us and the public, indeed also, the patients who receive our drugs. We uphold and support the idea that regulations should be in place. The pharmaceutical industry, of course, does that generally. We are a very heavily regulated industry. You cannot produce any pharmaceutical product without it satisfying regulatory agencies (the Medicines Control Agency in Britain) that the product is safe to give to patients and is effective. That is why, in fact, it takes ten years to develop a product and requires multinational and extensive clinical trials. That is right and proper. It is equally right and proper that manufacturing processes and R&D processes should be safe. We pay attention to all kinds of regulations in R&D, including those in the handling of radioisotopes, the handling of carcinogens, the treatment and welfare of experimental animals and so on. I could go on. The genetically manipulated organism regulations are therefore only part of the regulatory climate. I would say at the moment they are based in Britain on rationality, they are based on scientific judgment and as long as that persists we have no complaint, and indeed support and uphold such regulations. I think we are concerned about the danger that regulations could be put into place which perhaps are not based so much on scientific rigour but perhaps on some other some other view, some irrational, political or bureaucratic view of the world. I think we would argue strongly against that.

288. We have had written evidence from both companies, and as far as the questions are concerned you will enter in as you feel inclined, but the British Bio-technology evidence arrived too late for the Committee to have had an opportunity to have studied it closely so we may well ask questions you have already answered.

(*Dr McCullagh*) We apologise for that.

289. You are both relatively new companies obviously, since this is a fairly new industry (if I can use that word). If you were starting up in business today instead of six or seven years ago, in which country would you choose to be established?

(*Dr McCullagh*) Of course, that is a difficult question. From a business point of view, Britain, because I believe firmly and strongly that Britain lags "way behind" the United States in the development of biotechnology as a business. I think it has tremendous potential and I would like to see an industrial sector, based on biotechnology developed strongly in this country. I have to say that is one of the driving forces behind establishing our company in Britain and, indeed, locating in Oxford, close to one of the centres of prestige and learning in Britain and one of the biggest groupings of teaching hospitals outside London. Having said that, would we be better off; would we be able to grow the business more quickly if we established it somewhere else? It is possible, yes, that the United States might be a more clement environment in which to develop at this time but I think only because there has been a track record, a history of biotechnology companies actually developing, and, therefore, their regulatory approach has perhaps had more experience than ours. But I do not think the regulatory climate in the United States of America is sufficiently weaker than or different from ours as to justify relocating the company or even considering a change of location at the start.

(*Dr Birch*) I think we would share a very similar view. We would certainly take the view that there are still very good reasons to set up companies like ours in the United Kingdom, and is particular a very strong technical foundation. Certainly I do not think regulatory considerations would play any part in our deciding where we would set the company up. Other considerations—financial considerations, market dynamics—may play an important role but I still believe that there are good reasons to set up companies like ourselves in the United Kingdom.

Lord Flowers

290. Quite a number of British firms are sending their R&D activity at any rate somewhere else, especially to the United States. Why do you not want to do that?

(*Dr McCullagh*) Perhaps I can answer that. We are establishing this year a clinical and regulatory laboratory and office in the United States in order to conduct clinical trials in the United States, so we will have an international reach to our R&D as we expand and develop. But establishing a research laboratory in the United States rather than in Britain is more to do with whether you can access high-quality scientific talent in a particular area. If you have a particular piece of research which is better done in the United States because of operational reasons, that is more important in our minds in taking that decision than the regulatory climate in which that laboratory operates.

291. Would you say that basic research is sufficiently well supported in this country that there is no need for you to go elsewhere?

(*Dr McCullagh*) That is a different question. No, I do not think basic research is sufficiently well supported in this country by any means. I think the public funding going into the science base in this country would benefit from being increased and I think that as an industry the pharmaceutical

[Lord Flowers *contd.*]

companies and the emerging biotechnology companies would benefit from that, as, indeed, would the whole of Britain in time.

(*Dr Yarranton*) I would say there is a concern about the deterioration of the scientific base in the country due to a reduction in funding. I would also say, though, that obviously recruitment is international. We do have people we have recruited from abroad, so those well-trained professionals do move from country to country, hence one does not have to be based in America in order to recruit good quality staff.

292. Do you say it is deteriorating from your own evidence or are you just repeating what they say?

(*Dr Yarranton*) From the availability of trained people, yes.

Chairman

293. We were told by the DTI that nothing much had changed in the United States regulations, apart from the fact that they were now "user-friendly". I am wondering if you agree with that. Secondly, could you tell me what first-hand experience you have had of seeking regulatory approvals overseas, in the United States or elsewhere?

(*Dr Birch*) If I can comment on that first, we have no first-hand experience of seeking approval in the area of containment or deliberate release, so our only experience is in the area of drug regulations, where it is probably fair to say that the principles are essentially the same whether you are working in Europe or whether you are working in the United States of America. The details of the way in which those principles are enacted are different but essentially the principles are the same.

(*Dr McCullagh*) I think we share that view. The regulations that apply to us as emerging pharmaceutical companies primarily are regulations about the quality, that is, the safety and efficacy of the product, because it is for human use, of course, and it is quite right that those regulations should apply to it. The Medicines Control Agency in Britain and increasingly now through the Committee on Proprietary Medicinal Products (CPMP) throughout Europe are harmonising their regulations very much in line with the type of regulations that have been put in place with the Food and Drug Administration in the United States. So in terms of regulation of product there is quite good agreement about what are appropriate standards of safety and efficacy. Behind those standards are a series of guidelines, which are known as Good Laboratory Practice, Good Manufacturing Practice, and Good Clinical Practice. They have quite definitive statements about what constitutes good clinical practice, how you run a clinical trial safely and effectively so that the data can be believed and are valid. I believe that biotechnology would benefit from a set of guidelines that we might call "Good Biotechnology Practice", which could, in fact, emerge out of the current GMO regulations because, of course, the guidelines, which display the way in which risks should be assessed in the handling of genetically manipulated organisms, are indeed just that "guidelines". They are showing how you use good professional knowledge to assign risk and safety to a particular process, and I would like to see it emerge to that end. I think we are at a stage when you cannot just leave it to individuals or individual companies or individual scientists, but I do believe that the regulations currently in place, the new regulations, are essentially training the individual company to make the risk assessment, to report what they are doing and they are trying to provide guidelines for them to do that. I think that is the best way forward and I would be against any more specific regulations being added to them.

294. You are both relatively new companies; you are both expanding into a new area. Can you tell me if there are any strategic decisions as businesses which you have made in which the United Kingdom regulations have played a significant part in your decisions, and especially can you tell us whether the United Kingdom regulations have impeded your growth in any way?

(*Dr McCullagh*) I think it depends whether your question is directed specifically at the GMO regulations or whether you are talking about the regulatory climate in more general terms.

295. In fact both.

(*Dr McCullagh*) If I can take the latter first, to build a new business from scratch in Britain, particularly one involving new areas of technology and innovation, is not easy. It takes long-term investment and the support, therefore, of investing shareholders. A key and important factor to those shareholders is that they should get some value, a return on their investment, and until rather recently I think our Stock Exchange had not been very approachable in terms of listing a company which was reporting losses, it was in a development phase, and, of course, a pharmaceutical company has to invest very heavily in product development over many years to bring a product to market. We worked rather closely last year with the Quotations Panel of the Stock Exchange and the Executive to define a new set of guidelines to enable the Stock Exchange to admit companies such as our own to listing, and I am delighted that they have now published those guidelines and are bringing into force a set of regulations which will encourage in a better way than they have before companies that are emerging such as ours to list. So I could take a view and say that the Stock Exchange's view has hampered us in that we have not been able to go public until last year, some six years after we were formed, whereas if we were in the United States of America we would have been able to go public within 18 months and get access to public investor funds. But if I am honest, I can tell you that it has not been a hindrance because we have had very strong support at the private company stage from United Kingdom institutions and, indeed, I think we went public at an appropriate time. But I would like to see that regulatory climate loosened further and the Stock Exchange become more liberal in its readiness to allow new emerging companies to get access to funds. I mention that because it is part of the regulatory framework that affects the growth of companies like ours. The precise regulations on the manufacture and production of chemicals or biotechnology products are things that should not be a determinant of company growth. They should rather be something we should aspire to follow

[Chairman *contd.*]

professionally. They should be rigorous and should be appropriate. As I said before, they should not be based on non-scientific or irrational procedures.

(*Dr Birch*) Yes, we take a very similar view. I think looking at the very specific recent regulations, although we have some concerns that we indicated in our response, I do not think any of those concerns are sufficient that they would alter our strategic view of the world. In terms of regulations generally, particularly pharmaceutical regulations which are the regulations which occupy most of our time, I think the reality is that we as professionals gain a competitive edge by taking quality very seriously and dealing with those regulations efficiently and professionally. We have to deal with them on an international basis anyway and be as aware of the American regulations and be as able to meet those as the European regulations. I think in practice those regulations do not influence any strategic decisions particularly as to where, for example, the company might be based.

Lord Wade of Chorlton

296. In the Celltech report you twice mention a product which can be assessed as very low risk. How do you actually identify a product which is very low risk as against something that is a higher risk? At what stage of the process could you identify it to be able to say, "That's in a range of products that need not have the same regulatory control as this set of products"?

(*Dr Yarranton*) Certainly the majority of our products are fairly generic, in the sense that monoclonal antibodies are very similar. These proteins are almost identical and they differ in a very small region. These are proteins which are naturally found in you and I, and they are only active when injected into an individual and are not active if you eat them, for example. These are very low risk, very similar proteins. When we move on to other proteins which fall into different groups of proteins, for example, which can be involved in the initiation of cancer then we can see these as being a higher risk, and there are a whole family of these proteins. You can start to put the products, or the proteins we are dealing with, into categories, categories that are certainly of a higher risk and categories of a lower risk. Because of biotechnology, because of the technology that we have, it is quite clear now that we can define products in a lot of detail. We know an enormous amount of detail of the entities we are making. These are not crude mixtures of compounds, but highly defined entities, and we understand their properties very closely. That is how we can actually put these into low and high risk by definition. This is really the power of technology, to define products very, very clearly rather than to have a mixture of products where we do not really know what it is. It is being able to define both the organism and the product that allows safety to be adequately addressed.

Chairman

297. Low and high can be fairly subjective. Brave chaps have climbed mountains that I would not consider doing. Is there any way you could put numbers to it?

(*Dr Yarranton*) In a risk assessment we do that.

298. You do actually do 1:10m, or whatever it is?

(*Dr Yarranton*) Yes, that is right. For example, we can tell whether the organisms can transfer this DNA from one organism to another. We can actually reduce the risk by selecting an organism that cannot do that. We go through a procedure in which we evaluate the risk based on host/sector and product and put some figure on each, and then we obviously multiply those together and see whether that comes to a high risk or a low risk. By analysing risk in a segmented way we can actually look at low risk in a variety of categories and then look at the whole.

299. You have not been in business long enough yet to see whether your numbers are correct?

(*Dr Yarranton*) No, although recombinant DNA technology has been extensively used for 20 years without any suggestion of detrimental affects on those working in the laboratory.

(*Dr McCullagh*) Could I respond to Lord Wade's question. I think it is very important to be clear that the regulation of the safety of the product is already catered for in pharmaceuticals by the pharmaceutical medicine control regulations in place. You cannot start a clinical trial without getting a clinical trial certificate from the MCA, and you certainly cannot produce a product without a product licence, and until a marketing authorisation application has been approved. In order to do that the Medicines Control Agency satisfy themselves that the product is safe by looking at the data that you have developed in human clinical trials, and prior to that in animal toxicology studies, and prior to that in pre-animal studies in a laboratory. That applies equally well to a product derived from a biotechnology process as it does to a chemical entity from a chemical manufacturing plant. I think it would be entirely wrong if the biotechnology regulations extended to cover the product which is already regulated by a separate and adequate set of regulations run primarily by the Department of Health. The situation is analogous to health and safety regulations surrounding the manufacturing of chemicals, whether they are carcinogenic or whether they are pollutants etc. and the care to be taken in such plants. Biotechnology production regulations should similarly pay attention to the guideline, is there a risk in manufacuturing? Or is there a risk in the handling of the product? I think that that is appropriate, but not to go further.

Lord Wade of Chorlton

300. The point is that this is a question that has been raised by a number of people both in this room and on other occasions. It would seem to me there is a need to actually be able to identify those products which can be clarified in such a way that one can sit down with the regulatory authorities and come to a clear way ahead that both sides can understand exactly what you are talking about. At the moment

[Lord Wade of Chorlton *contd.*]

there seems to be no clear way where everyone can agree on the way ahead, and that seems to me to be necessary, particularly when talking about encouraging newer companies because it is clearly in that area where people want to make quick progress in what I would call the soft end of the market, rather than the hard end of the market. Do you agree that there is a need for industry and the regulatory bodies to get down and define that position more clearly?

(*Dr McCullagh*) There is nothing in principle different from a product derived from biotechnology and a product derived by a chemical manufacturing process. Both the public and the receiving patient must be assured that that product is safe. If not we are going to have a repeat of the Thalidomide disaster, for example. It was Thalidomide that led to the strict regulations currently in force. I think, having had those regulations in place, the whole industry has attuned its product development processes to satisfy very stringent criteria of efficacy and safety. I think the manner of production, the licensing of the production plant, and the implementation of good manufacturing practice guidelines in production are all part of satisfying safety under those regulations. I think we have to put some limits around what biotechnology specific regulations should try to encompass. I think they should be regulations which require appropriate containment and care in the handling of genetically manipulated organisms as a process, and not concern themselves specifically with the product, which is already regulated by existing legislation. I am talking here, of course, about pharmaceuticals, and what I say may not be appropriate for the agricultural industry.

Lord Soulsby of Swaffham Prior

301. Could I go back to something you mentioned earlier, and also to a paragraph in your submission which says that United Kingdom biotechnology lags far behind US biotechnology. I want to put that with reference to another comment you made about the science base in this country, which is not really serving the needs of biotechnology. I can recall with great difficulty trying to find post-doctorals that were biotechnologists because they were all disappearing to North America. What is the way ahead to resolve this? Do you have any commentary to make on whether this should be a central government supported effort or should this come through private industry? Do they have a bigger role to play than they had in the past?

(*Dr McCullagh*) I think the simple answer is that both should attempt to encourage and support a growing basic science base in Britain. As regards biotechnology, biotechnology is a convenient way to describe a variety of scientific disciplines which spread from animal pathology through to small organisms, microbiology, through to chemistry and innovative techniques in building and making and understanding chemical interactions at the cellular level. I think, therefore, biotechnology does not exist in the universities as a science, as a subject. "Biotechnology" is a word that should be used to describe the application of a wide variety of modern sciences to producing biological products on an industrial scale that are useful and helpful. Therefore, I think we should not be looking to establish departments of biotechnology at the universities. I believe we should be encouraging increased funding into the continual pushing-back of the frontiers of knowledge in medicine, biochemistry, chemistry, biophysics and so on. The process of doing that, of course, is fundamentally in Britain one where the support is coming from the universities themselves and their funding sources, primarily from public funds, but I think it is important that industry plays its part as well. Even though British Biotechnology is a small emerging company we are spending this year in excess of £1.3 million on supporting research in British universities under collaborative programmes where both the university and ourselves benefit. These programmes support post-doctorates, scholarships, laboratory workers in the university, and, of course, the technology transfer process that enables the university and ourselves to benefit from products that arise. To put that £1.3 million in context, we are a small company and that is about 6.5 per cent. of our R&D budget. It might be appropriate to spend more and if the scientific base were there that we would find attractive support, we might spend more. Therefore, it has to be a collaborative partnership between industry and public funding.

302. What about others—Celltech, for example? Are you doing the same?

(*Dr Yarranton*) Celltech has been involved in a variety of the link schemes which try to bring together academia and industry, and it has also had a very strong record in funding research in universities. I would say by looking at the American model and the way in which the American biotechnology industry has evolved over the last ten years, that really has happened not necessarily by direct transfer of technology from the universities but by people within the universities setting up small companies. I think one thing that could be promoted within this country—I am not quite sure how it could be done—is to promote that type of activity. I think academics setting up small companies really would fuel the biotechnology industry in this country and for that to happen you need a very strong academic base, very good investment in research, and in research institutions in this country.

(*Dr McCullagh*) I think there is another point, you need companies which currently exist to set an example. I think Celltech and British Bio-technology are the two leading biotechnology businesses in Britain. You need them to be successful. When others in universities see the successful generation of product sales the growing financial development of the company, they will be encouraged to follow in our footsteps. So how we succeed will affect how others see the opportunity. I think that university academics are often somewhat afraid to go out into the commercial world because it is not something that they are used to and I think having a path to follow is important.

303. Of course, there are a number of universities that have set up their own internal companies to facilitate this, which helps very substantially?

[Lord Soulsby of Swaffham Prior *contd.*]

(*Dr Scott-Ram*) I think there is another area which is important and that is intellectual property in relation to university technology transfer. In the United States there is a very strong history behind technology transfer on a strong approach to patent protection and the ownership of such patents by universities. In the United Kingdom there is a much more uncertain position and different universities take different positions on how they handle patents, and on whether or not to patent. We feel that a strong approach to intellectual property in relation to universities would help that as well.

(*Dr McCullagh*) Another recommendation or suggestion I would have in order to aid technology transfer and the establishment of new companies spinning out from universities, is really to have a more favourable investment environment and taxation environment for such companies. Certainly relief from capital gains tax for the investing institution or entrepreneur on his investment would be attractive. Perhaps, however, more important for us as a developing company is the timing of tax credits on R&D losses. At the moment, of course, we have carried forward substantial R&D losses on our P&L account but we cannot benefit from them since we are not in profit. If we could take the tax credit in the year when the loss on investment was incurred, it would be a major benefit in assisting us in more rapid development. I think that single change in the taxation law as it applies to innovative high-growth companies might instantly change the way in which institutional investors, venture capitalists and academics view the opportunity for biotechnology companies.

Lord Flowers

304. Could I ask Dr Scott-Ram something. He said something that interested me very much about the university policy towards patenting and all that. You are right, of course, that the universities make up their own minds on how they are going to handle matters like that these days. Some of us have had to fight very hard to enable them to have the right to do that. Are you suggesting that one should go back to the days when there was a centralised authority, the forerunner of British Technology Group, known as NRDC?

(*Dr Scott-Ram*) No, quite the contrary. I would argue that each university should make up its own mind on how to deal with it. It is just that if we are looking to bridge the development gap from a university to industry, there has to be a stated policy and a positive attitude to patent protection such that there is an adequate transfer of that intellectual property, and if universities are seeking funding from industry or venture capitalists to set up a company, then the only thing the flat investment is going into originally are those intangible assets vested in that intellectual property. I think this has to be clearly defined and understood by universities. So I would not advocate a return to a centralised body at all.

305. I am glad to hear that, but do you think some universities are treating patenting too lightly?

(*Dr Scott-Ram*) There is a big difference going from university to university, I think, in terms of what they believe, can and cannot be patented and I think much of this is controlled by the amount of finances they have. I think it is a vicious circle. However, I think in many universities current levels of investment in intellectual property are far too low.

306. Is there any evidence that you have that the country has lost out because of that?

(*Dr Scott-Ram*) There are examples such as the monoclonal antibody patent area in the past. When I look at the United States university applications compared to the United Kingdom ones, there is a much more aggressive strategy in patenting, which is partly due to the strength of the United States Patent Office in relation to what they set for their standards and what is patentable subject matter compared to Europe. So much of it comes down to patentable subject-matter as well. I will say in some universities there is a very high standard. It is just that I think it is still variable across the board and that encouragement should be given to universities and academic institutes to pursue sound patenting strategies.

Chairman

307. This is quite an interesting area we are in. I am wondering how much more important to both your companies the sort of things we have been talking about in the last few minutes are than the regulations themselves?

(*Dr McCullagh*) Yes, is the answer.

308. They are more important than the regulations?

(*Dr McCullagh*) Yes.

309. Let me ask a quick question about the regulations because we want to know something about them. The DoE have told us that the difference between horizontal and vertical is academic. I know that some of my colleagues in the Committee would prefer to talk about process and product but I am willing to stick to horizontal and vertical. Do you think it is academic or do you think it is not? Is the DoE right?

(*Dr McCullagh*) As regards the contained use regulations as they affect the pharmaceutical industry, then I think that attention should be paid in the way I have already made clear to regulations applied to the product and a separate set of regulations applied to the process. The process regulations are the biotechnology regulations and the product regulations are those which are concerned with the safety and efficacy of drugs, and those regulations are already effective and in place. I think it is very clear cut, therefore, for pharmaceuticals and pharmaceutical manufacturing. I think the regulations are appropriate at present. I do not believe they should become more complex. There is a tendency already for them to be complex, confusing in part, and I think they could be simpler, but I make no other comment about them. They are acceptable. I do not think that necessarily applies to deliberate release, where I think there is more of an overlap between horizontal and vertical but the principle should be the same, that one should try to restrict biotechnology regulations to covering the product development and manufacture and leave others to assess product safety on proven tests.

[Chairman *contd.*]

(*Dr Birch*) We would take a very similar view. We are very happy with the present arrangements where the product is regulated through a national authority and the health and safety of workers is separately regulated.

310. You are not bothered about having two different agencies?

(*Dr Birch*) No, we find it works very well and it seems very logical to us. The issues and the risks are rather different in the two cases, and it seems perfectly sensible for us to treat them separately.

Lord Flowers

311. Could I just ask you what your attitude is towards the influence of Europe, the Commission in Brussels, on the whole regulatory mechanism? Does it affect you in practice?

(*Dr McCullagh*) I think it does, yes, and I think it may do so more. The current British regulations of course derive from EC Directives and there are in draft at the moment a substantial number of EC Directives being discussed which may affect in a very conflicting and confusing way the production of biological entities for human use and industrial products. I think we are concerned to make sure that, as far as Britain is concerned, the implementation of such Directives are based on principles of sound and rational science and realistic concerns about safety, and not on bureaucratic or other concerns.

312. You have not actually said that you find the Commission is bureaucratic in the way it handles the problem, but is that what you meant?

(*Dr McCullagh*) No, I am not saying that. I am saying that there are a large number of draft regulations being discussed not all of which we would support or feel are appropriate.

(*Dr Scott-Ram*) There is also the question of interpretation on a national level. While the aim of having a level playing field for all regulations is very commendable, I think there are going to be national differences in the interpretation of those regulations, or at the very least there is the potential for that.

313. Which will affect competitiveness?

(*Dr Scott-Ram*) Yes, it would affect competitiveness. For example, in one country, regulations may be interpreted slightly more leniently for a variety of reasons. For example, different interpretation may arise through the different political systems in operation, or through the different legal systems. In the United Kingdom, our legal system is based on "common law", which in France it is based on "Napoleonic law". The different interpretation undere these systems could affect competitiveness.

Chairman

314. Are you able to make any real input into the discussions which are going on on regulations?

(*Dr McCullagh*) Both Celltech and ourselves share a route of influence through the Senior Advisory Group on Biotechnology, which has been putting views to the Brussels Commission on these regulations. We also, through industry associations in the United Kingdom, have been making representations about what industry would favour, and that is, simple and clear regulations and those based on a realistic assessment of the risks.

315. Is this a satisfactory route? Does it produce the results you want?

(*Dr McCullagh*) It has so far been satisfactory, but I am not sure that it will always be so. Our concerns therefore are prospective. We want to make sure that new regulations do not inappropriately constrain industry and its competitiveness. If you are asking whether we would wish to be consulted more before new regulations are imposed then the answer is clearly, yes.

316. Are you both agreed on that?

(*Dr Yarranton*) Yes.

317. Thank you very much, gentlemen, it has been most interesting. You will see the transcript in due course, and if you wish to add to what you have said or correct any comments you have made we will be very pleased to hear from you. I for one would quite like it if you would give a further comment on the matter of patents and so on in writing.

(*Dr Scott-Ram*) Certainly.

Chairman] Thank you very much.

Memorandum by the Agricultural Genetics Company Limited is printed separately

Examination of witnesses

PROFESSOR P BOSELEY, Director of Research and Development, and DR R H GILMOUR, Chief Executive, Agricultural Genetics Company Limited; and PROFESSOR C POLGE, Research Director and MR A TALBOT, Process Development Manager, Animal Biotechnology, called in and examined.

Chairman

318. Good morning, gentlemen, sorry to have kept you waiting. Would you please be kind enough to identify yourselves. If you care to make a short statement about the attitudes of the respective companies we would be very pleased to hear from you.

(*Professor Polge*) I am Professor Chris Polge from Animal Biotechnology. I am a founder and Director of that company. The company is about six years old and it is largely venture capital backed. A large part of our work initially was devoted to developments in animal embryology, technology transfer mainly from the AFRC, Institute of Animal Physiology and Genetics Research, and our business was related to the development of new techniques in animal embryology which could be applied to advance animal breeding, principally through the route of embryonic transfer. This involves the large scale

[Chairman *contd.*]

production of bovine embryos for extended use in embryo transfer; opportunities to provide embryos of pre-selected sex; and, in the longer term, opportunities for being able to create multiple copies of embryos through processes of nuclear transplantation; and, longer down the line, possible opportunities in genetic modification of animals, because the technology that we are developing is the key to be able to introduce very specific genetic modifications if so desired. Another part of our business which we have been developing more recently is devoted primarily to the human health care area, and this is perhaps an area where we are more concerned with regulations related to genetic modification. I should say that our agricultural business is mainly regulated by new Acts which control embryo transfer. That part of the business does not really involve so much genetic modification. In the human health care area we have positioned ourselves in an area in which we are developing genetically modified cells and cell lines which can be used for the screening for new drug discovery, rather than using these cells for producing a product. These very much fall into the area of contained use. Another area of application is deriving genetically modified animals as models for human disease, again in relation to opportunities for the development of new drugs. Mr Tony Talbot is our Process Development Manager. Whereas my role in the company is more identification of opportunities and painting the broader brush strokes, Tony Talbot is the person who is more concerned with interpretation of the regulations which may concern us.

(*Dr Gilmour*) My name is Roger Gilmour and I am the Chief Executive of Agricultural Genetics company. You have heard of technology transfer companies. We were set up as a biotechnology transfer company. So in 1983 we were set up with the specific mission of identifying useful research in the Agriculture and Food Research Council research institutes and organising the transfer of that research into products into the marketplace. So we act as the principal commercial arm in plant biotechnology for the AFRC. We also work with universities. We have our own research laboratories where we use the techniques which have been developed. We use them to create, for instance, genetically modified plants. We do not do pure research ourselves. We depend upon the universities and the research institutes particularly in the United Kingdom as the source of research, so we work closely with them. I think that makes us rather unusual in our area. We were started in 1983; we raised our funds mainly from the venture capital market in November 1984. The state of development we are at just now is that this year we will be marketing six products in the marketplace. Two products are natural fertilisers, one bacteria, one fungus, both of them from the AFRC in origin. Two products are natural ways of protecting plants from insect attack. One of these is a bacterium and one is a microscopic worm. Again they both came from the United Kingdom research base, and we have two plant varieties from our plant breeding programme which we will be marketing this year. We are also involved in genetically modifying plants and the state of development there is that we have one plant which is in field trials this year. That is an oilseed rape and it has an insect-resistant gene from another plant put into it. Professor Boseley is in charge of our R&D Department, so he has the responsibility not only of supervising and organising our own R&D but also, very importantly, of liaising with the research base in the United Kingdom. These regulations for us are very important. The whole company is based on biotechnology, so the rules and regulations which say what is allowed or is not allowed or how it has to happen or the cost of the time involved in making it happen are basic to our whole company.

319. Thank you very much. We have had a paper from Agricultural Genetics. It may be that some of our questions will have been answered already. I would like to start by looking at the very full answer to question 8, which compares the current regulations with those elsewhere, and right at the end you say: "The only major countries which have adopted a sensible registration system are France and Canada which should be emulated by the United Kingdom." Does that apply only to fertilisers and only to natural fertilisers or were you thinking rather more widely when you made that comment?

(*Dr Gilmour*) We are thinking in the wider sense. We are looking at the use of biological methods of feeding plants and of controlling plant disease and infestation, but not many countries have organised systems of approval and systems of judging whether or not your claims are correct, or whether the product that you are selling actually works. There are two countries that are different, France and Canada, where they both have specific approval independent systems which take your products and test them and say whether or not they work.

320. This is over the whole range, is it?

(*Dr Gilmour*) This is specifically in this area of biofertilisers.

321. And you think the United Kingdom should follow down that line?

(*Dr Gilmour*) We think that generally Europe should, yes.

322. Europe?

(*Dr Gilmour*) There should be standards which everyone has to meet.

Lord Wade of Chorlton

323. You mentioned in your report the fact that you have been involved in extra costs because of the DoE regulations. Could you give us some idea of what we are talking about in terms of those extra costs?

(*Dr Gilmour*) I think the costs occurred in two different ways. It is not particularly because of the DoE; it is because of the whole regulatory system. First of all, you have the actual cost of the routine that you have to go through and how much money you have to pay. That is really not the most significant part. Then we have the cost in time and for large companies it is quite easy for them to devote management time to inputting into the development of the regulations. For small companies it takes a considerable effort, but most importantly, the cost

[Lord Wade of Chorlton *contd.*]

that we have in time is the cost of product opportunity and that cost arises in the development of corporate strategy, that it takes so long to develop a new plant product or a new micro-organism that you are making the strategic decision on what to do or what not to do at a time when you do not know what the regulatory environment will be. There we have made strategic decisions early on in the development of the company which will dictate the company's future direction.

324. Is your experience similar in Animal Biotechnology?

(*Professor Polge*) As I say, I do not think we have a similar experience because our business in the embryo transfer field has not been governed by the genetic manipulation regulations. We have witnessed in the recent regulations that have been enforced in relation to embryo transfer which are based primarily on EC Directives for the purpose of controlling how embryos are produced from the point of view of animal health, and particularly in this country, how embryo transfer is carried out. We find that in Britain probably these regulations are harsher than in some other European countries because they are based very much on perceptions of animal welfare which have empowered veterinarians to make decisions on whether a certain animal will be able to carry a calf effectively to term and bear it naturally. So all animals as potential recipients have to be inspected by a veterinarian. I think it is going to be very difficult to enact effectively, very difficult for the veterinarians to have to take these decisions. Another procedure is the use of epidural anaesthesia for carrying out the embryo transfer and this has involved a change in the Veterinary Surgeons Act to enable lay people to carry out epidural anaesthesia under veterinary supervision. This has involved the setting-up of a training programme in the University of Cambridge to license lay people to carry out these procedures. So the development of our business has been affected to some extent by these new regulations. In the area of genetic manipulation of cells for drug discovery, I think it is true to say that our company has been very much influenced by taking the strategic decisions on the need to be able to develop relatively quickly with the limited money that is available through investment, through the venture capital route, and to position ourselves in an area where we are not looking to having to produce a product and get that passed through all these regulations but rather producing cell lines which are an enabling technique for the discovery of new drugs.

325. You have both at separate times described the regulatory climate as "harsh", Professor Polge just now and Dr Gilmour in the written paper. Can you tell me whether the regulatory climate could be made less harsh but safely, and how?

(*Dr Gilmour*) I would just like to emphasise from the outset that we fully realise, accept and endorse that with any introduction of a new technology there has to be assurance that it is safe, and in any comment I have that is the overriding concern. I think we have to be careful that we do not lose our sense of perspective. Plant breeding is not something that is new. Plant breeding has been going on since the first grasses were taken and grown as crops. Over a period of years there have been different ways that have been discovered on how to increase the amount of variation that you get into plants, how to get the genes to jumble up and recombine in different ways, and how to take parts of chromosomes that carry a useful gene and to insert these chromosomes. These things have been done and have resulted in plants which have been sold and marketed today, which are widely accepted and which are generally recognised as being safe. When the next step comes along where we make use of this gift that we have been given of being able to target and take one specific gene, I realise we have to make sure that what is done is safe; but it is very unclear as to why there should be any expectation that it should be other than safe given all the work that has been done that involves greater genetic change than specifically targeted genetic change. What we would like to see is our continuing to have independent assessment of safety, and assurance of safety, but we would also like to see within that safety assurance a move as rapidly as possible to identifying the techniques and the steps which are safe and to allowing them to become part of the normal process of plant breeding and of the creation of agricultural products, which would then be subject to the normal regulations. We do not see that this should be used as an excuse to throw away what has been developed over many years of a regulatory system which has everybody's confidence. It is only one new ingredient, and we should stick with the system which has evolved of legislation by product, with the regulatory bodies within the government staying the way that they are and not have this being used as some reason for sudden change.

326. People's perception of plants and animals is somewhat different. What are your views?

(*Professor Polge*) When I was describing the regulations as "harsh" perhaps I could modify my words to say "more stringent" in the United Kingdom than some other European countries.

327. I do not mind the word "harsh".

(*Professor Polge*) It is quite a good old English word.

Lord Flowers

328. Do you mean more stringent—

(*Professor Polge*) More stringent from a perception of animal welfare.

329. But more stringent in principle, or more stringent in the way they are applied in practice?

(*Professor Polge*) I do not think they exist in some other European countries. I think the same regulations have not been made.

(*Mr Talbot*) Could I just add to that, the regulations as they seem to have been applied to new technologies, and I am thinking particularly about the embryo transfer work, actually effectively penalise the new technology of breeding because they are more stringent than the existing controls on selection for breeding using either natural service or using artificial insemination. We feel there is an extra hurdle, if you like, for the new technology to be adopted and to be used. This is something we should look out for and be aware of with new technologies;

[Lord Flowers *contd.*]

that they should not be penalised over existing technologies, unless there really is a real additional risk associated with them.

Chairman

330. Does it arise to some extent from the use of the term "genetic engineering"? As an engineer this hurts my feelings! The notion of genetic engineering somehow suggests that man is meddling in some natural process in some way. To all intents and purposes, you think it is no different from the kind of selective breeding both in animals and plants that has gone on for generations?

(*Professor Polge*) No, I think both in plants and animal breeding opportunities are provided through genetic manipulation that are not available through natural breeding processes, so it is different. Everybody wants to ensure the safety of any procedures that are involved and how they affect the environment and the wellbeing of the human.

331. If the new system is different why should the regulations not be more stringent?

(*Professor Polge*) They should be based on a very clear assessment of risk, and the same assessment of risk has to be applied to that as to other procedures. If one takes, for example, this regulation relating to embryo transfer, embryo transfer has been singled out because it is different from natural breeding yet there is no regulation which controls the farmer in the choice of a bull that he uses for breeding a certain animal or for the choice of the semen that he selects for breeding that animal. Embryo transfer has been selected as a specific case without perhaps a true assessment of the risk involved.

Lord Walton of Detchant

332. Could I clarify a couple of points about the issues we are now discussing. The first relates to the implications and applications of the EC Directives 90/219 and 90/220 where I think you said, Dr Gilmour, you regard these as being potentially over-bureaucratic. I would like to have some evidence or examples of the extent to which they are. The other point I would like to raise with Professor Polge is, this regulation to which you refer relates to embryo transfer, is this derived from those EC Directives, or is it a purely United Kingdom based regulation which is quite separate from the EC requirements? That is the point I wanted to have clarified.

(*Professor Polge*) There was an EC Directive relating to control of the production of embryos mainly from an animal health point of view, and these were harmonised in the European countries. I believe that our regulations controlling the conditions under which embryos are produced, either from a living animal or in vitro, are similar in European countries. I think additional legislation was brought in in Britain controlling embryo transfer based on animal welfare concerns.

Lord Soulsby of Swaffham Prior

333. Could I return to the question of animal welfare. I take your point about the stricter regulations being based on what might be the irrational perception of poor welfare as a result, say, of embryo transfer, but there is a general theme that seems to be around in the public perception that all genetic manipulation biotechnology is not good for the welfare of animals, which I would regard as totally irrational. But can you perceive altering this general public opinion by the benefits that biotechnology do, in fact, bring to animal welfare? I can think of many but have you a concept that what you are doing in the agricultural area with animals and with plants, for that matter, does, in fact, enhance animal welfare rather than detract from it?

(*Professor Polge*) Yes. I think one example is the opportunity to use these technologies to introduce better disease resistance, for instance. This would have a huge influence on animal welfare and be very beneficial indeed, and that is one of the objectives of this type of technology.

334. That tends not to come over to the public, and hence I think you get these more stringent regulations often triggered by public opinion or by the public opinion of a small group of the public, when, in fact, if they were exposed to the more general knowledge that vaccines and improved resistance and so on would bring they might not think that way. Is there a case for doing more PR work?

(*Professor Polge*) Indeed, I think that applies to the whole of the biotechnology industry. I am a member of the Biotechnology Joint Advisory Board and increasing public awareness of science and particularly biotechnology is a major concern of that committee. It is very important that the opportunities that biotechnology has in developing new wealth-creating opportunities for the building of new businesses is not going to be suppressed through a misunderstanding or a lack of understanding of people generally about the risks involved, and I think there should be far greater discussion and open debate opportunities for a fairer presentation within the media and so forth of the whole of these issues to improve the climate in which these types of technologies can develop.

Chairman

335. Dr Gilmour, I must apologise to you because I was a bit quick on the trigger and I kept you from Lord Walton's question before you had a chance to answer it. Can you remember what the question was?

(*Dr Gilmour*) Yes, the bureaucratic aspects of the regulations.

(*Professor Boseley*) Can I answer Lord Walton. What we are concerned about is that in our present form-filling exercise we have something like 89 questions to fill in just to put in a submission for a release of a genetically modified plant in the United Kingdom. We believe that could easily be simplified and, in fact, there are three Member States, including the United Kingdom, trying to do just that. We know that filling in such a form from our colleagues who are trying to do exactly the same, exercise in the United States and other countries, including France, at this present point in time find the form they complete is half the size. As Dr Gilmour has already indicated, a large proportion of time can go into this very exercise and this is only one stage of the process of putting a product on to the market. So the last thing we want to do is to increase this from filling,

[Chairman *contd.*]

which is a waste of paper as well as being an "environmentally unsafe sort of thing" anyway, and increase the amount of time and money involved in actually submitting what we call a satisfactory procedure where all safety precautions are already in place.

Lord Walton of Detchant

336. Did a scientist design the form or did a committee?

(*Professor Boseley*) This was a European Community regulation. The other thing I would like to state is that what we do want to do is move ahead through experience. We do have a large number of field trials taking place worldwide at the moment, well over 1,000 field trials. With that experience, Lord Walton, I believe we can use that experience to simplify the procedures. It is already taking place in the United States. The USDA have already set up a notification procedure for certain crop plants where they have gained that experience. We want to see that same level playing-field in Europe and I hope the United Kingdom will embrace that sort of simplification.

Chairman

337. I wonder if you can tell me, since many of your products will be developed and marketed under the deliberate release regulations, what problems you foresee for, firstly, transgenic plants and, on the other hand, transgenic animals under the 1992 regulations?

(*Professor Boseley*) Can I follow up on the transgenic plants because I think it is an extension of what I have been saying. Once we have shown through the exercise of field trials for transgenic plants that the product is safe, we then have the consideration, of how do we take that product to market. In the United Kingdom under the present review of new plants we go through what is known as National List Trials. This is a standard procedure where you verify that your new variety of oil seed rape or new variety of wheat has a certain advantage. It is declared so-called DUS (distinct uniform stable) and it is over several years that this actual procedure takes place. You can imagine that we need to have in place before that genetically modified plant goes into that procedure a clearance saying this is now safe, so that it can go through what we call normal vertical product legislation. We have to have that in place and recognised by other Member States in the European Community because they have very similar breeders National List Trials in the same way. This is one of the concerns I have, Chairman, that we have to have that agreement. I am not saying this will not be agreed in the United Kingdom but it has to be expedited quickly. To pick up Lord Wade's point, you have to prepare budgets well in advance if you are going to be able to do that. What are the costs associated with that? Is it going to give you a return on investment? We need to know that and that is why these regulations are having the effects that we describe in our submissions.

(*Mr Talbot*) As Professor Polge has mentioned, our main area of interest is the contained use of genetically modified organisms, and the products that we are most interested in are really tools for research rather than products that will be for general distribution. These products will be used under controlled conditions, but if they are products that are going to be sold they will still need to have product approval. We have had discussions with HSE in general terms about what this will mean and how it is likely to be approached and clearly it is something which we will be learning as we go through and evolve methods of describing the products. But I think we must recognise that difference between a product for general use and a product for contained use as a research tool. This is a very important distinction and we should build it in as early as possible. It should be easier to get product approval or a research tool because of the nature of the customer or the client who will be using it. That is one important area. The other issue is the costs generally for whatever the regulations require and whatever information is required to be put together. There is a significant cost however it is done and that cost tends to snowball as you look through all the different regulations you need to comply with, whether it is applying to the Home Office for use of animals or animal facilities, or HSE with the general safety regulations and so on. There are a large number of regulations and while we would agree very strongly and feel very strongly about the importance of safety, particularly the safety of our staff, I have concerns that with the welter of regulations there are we are in danger of missing any true hazards that there might be. We have seen this in a number of the other safety regulations, that there are some real hazards, some significant hazards, which need to be highlighted and pinpointed, and in which people need to be trained, and we need to make sure they do take adequate procedures for protection. But as the number of regulations and the number of controls increase, there is a danger that we will lose sight of the real hazards. We try and keep our eye on the ball to make sure we do identify and do make our staff aware of the real hazards and train them accordingly. I think it is quite difficult to do that and it becomes more difficult as the regulations become more complex. In a way you need a route map through the regulations to tell you what regulations apply and how and what the key ones are. I think such a route map would be very useful both from the point of view of companies that have to operate to those regulations and from the point of view of the general public, to understand what is actually going on, because I think, as Lord Soulsby has said, there is a general misapprehension about a lot of the regulations that there are or perhaps it is not even appreciated that there are regulations and controls in place. I think it is important from the public perception and for the efficiency of working of businesses that there should be a route map that takes us through these regulations and makes it easy to understand what the important issues are, and to keep regulations as simple as possible when it comes to the applications for release or for product approvals.

338. I am beginning to get the impression that neither company are fully satisfied with the regulations as they stand. I am told that some of the European regulations are under discussion and

[Chairman *contd.*]

might possibly be amended. What steps are you taking to make an input into these discussions, and how do you think you are getting on, if you are?

(*Dr Gilmour*) We are members of the Senior Advisory Group for Biotechnology. I make representations through the CBI. I have got an involvement with the Biotechnology Industry/Government Regulatory Advisory Group. We also belong to the British Society of Plant Breeders. Through all these avenues we are making our views known. I would like to say, first of all, that the government representatives go to great pains to ensure with companies like ours, small companies concentrating on new aspects of the business, that they listen to what we have to say and they give us a fair hearing. Similarly, with the major companies who are involved in organisations such as the SAGB, we give them full credit that we are treated as equals. So when they listen to the views on what should happen in Europe our opinions are treated with the same respect as the opinions from the largest companies in Europe. We are very happy with the opportunities provided.

(*Professor Polge*) In relation to the embryo business, we have had close liaison with the Ministry of Agriculture and with the Royal Veterinary College. We have not always won our point. In relation to genetic modification regulations, we have not been so concerned with the debate, to date.

339. Do either of you feel that these submissions are being effective? Are our ministries listening to you? Is Europe listening to you?

(*Dr Gilmour*) I think in terms of our government officials, yes, they are listening but obviously they do not always agree. They do listen and they do discuss and they do change their opinion and are willing to change their point of view, and you cannot ask for more than that. In terms of Europe, you move out of reason into a political climate, and it is a question of the political way to play the game there to reach your objective more than commonsense.

Lord Wade of Chorlton

340. Coming back to the issue of public acceptance, which Lord Soulsby raised, in one of the papers you refer to the need for an independent body. I would be very grateful if you would enlarge on that idea, and who would fund it and who would deal with it. I would be interested further to hear from Professor Polge because your company is in an area which many people could be the most nervous about. I personally would not support everything you are doing, but at the same time I could see the way the public could have that presented to them in such a way to spoil their image of biotechnology of all areas. Although you mention your concern about public perception, I would be interested to know how specific issues could be done and who should do them?

(*Professor Boseley*) What we are trying to get to grips with is the concern that the public have over, for example, labelling issues. For example, if I described how we would get a genetically modified wheat which is very safe but it has a flour which can be obtained from it when you grind it up. If we were to go to a product made from that flour, do we have to go to the food labelling system saying "this is made from a genetically modified flour"? What would be the repercussions of that? What we need is to have a body, which the public can go to, to say, "There are no problems associated with that. It is a safe product and everything has been tested beforehand". We are trying to take the emotion out of who is actually going to inform the public. Is it going to be vested with interests from industry, which they would be suspicious about, or is it going to be some other government or industry association? This independent body has to have a balance of people, where the public can go and ask for independent advice. That is what I was trying to get across.

341. Who would fund it?

(*Professor Boseley*) It is a difficult question to answer off the top of my head. It would probably be able to be funded by all of those—government, industry and so forth—but it should be seen to be a truly independent body where it is useful for all those sectors to have that information from it. I think it is only in that way, by working together, that you try to get to grips with what you would say is our next concern, which is the public perception of biotechnology.

(*Professor Polge*) I believe that it should be an independent body, because if they are purely industry based they are automatically suspect. There are organisations which already exist which I feel could be expanded, particularly the committee for the public understanding of science, which is supported by the Royal Society, and is perceived to present science issues in a dispassionate way. I think public funding and industry funding could go into supporting more organisations and more situations in making available and widening the debate on the public understanding of science. That would be most beneficial and should go right down to providing information for children in schools, because one sees that school children are being showered with leaflets and information from various pressure lobbies representing an alternative point of view. You see a perception building up which needs to be more balanced, I believe. It is very important for the development of this industry that this is done.

Lord Soulsby of Swaffham Prior

342. If I could go back to the United Kingdom regulations versus European regulations, much of the input there is from our various ministries and departments. Do you feel that they are supportive of your standing in biotechnology and what you want to do, or do you have difficulty convincing them to put your case in Brussels?

(*Dr Gilmour*) I would say that they listen and they will put your case inasmuch as they agree that there is a case that should be put, but they are not there to automatically act as a conduit for what industry thinks, but rather their interpretation of what is reasonable. I think the degree to which they are successful remains to be seen. I do not understand exactly how Brussels works. It is actually the difference between what happens in the Council and what happens in Parliament and the competition between them both, and we depend upon our government officials in knowing how to play that. We

[Lord Soulsby of Swaffham Prior *contd.*]

will have some idea on the degree of success when we see what the final outcome is.

343. But there is good consultation between the biotechnology industry and the Government?

(*Dr Gilmour*) I believe there is excellent consultation. I am very impressed by it.

(*Professor Boseley*) I think, Lord Soulsby, it is helped through the competent authorities. They have these meetings with their equivalents in the European Community and I think that is helpful. We mentioned the simplified procedures earlier on. It is through those competent authorities that I think we will get a better set of regulations. What I am obviously concerned about is that we do get industrys input into those competent authorities and they can take it forward understanding some of our problems. I think that is behind your question and I am hoping that through better dialogue with those people we are actually achieving it.

344. And on the animal side is it the same?

(*Professor Polge*) Yes, I would agree with that.

Lord Walton of Detchant

345. Professor Polge, I was intrigued by your comments upon the relationship of your work to human health and the possible work on animal models. Is your company one that will be proposing, for example, to explore the development of vectors for gene therapy in animal models of inherited human disease, and is this one of the fields into which you are likely to be moving as a result of your work?

(*Professor Polge*) More in providing animal models where one could test these sorts of things such as gene therapy. One has seen very recently an example of an opportunity perhaps to be able to treat cystic fibrosis by a gene therapy approach. This was made possible by, first of all, having identified the gene and then introducing that genetic modification into a model mouse and then showing that gene therapy type of treatment could reverse that defect.

346. I appreciate that. The point I was trying to get at is that there are some animal models of inherited disease, for instance the MDX mouse, the red setter dog that had a muscular dystrophy which is virtually identical to the human X-linked disease. I was wondering whether, in those particular animals, you are going to be helping those who are wishing to develop vectors to carry the missing protein into the cells?

(*Professor Polge*) I think one of the problems is that for many diseases there are no animal models, so hopefully we would be assisting those who are interested in developing such vectors by providing new animal models.

Chairman] Thank you very much for coming this morning and speaking to us so frankly. You will see the transcript and if you wish to add to it or modify it in writing, please do.

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MINUTES OF EVIDENCE
TAKEN BEFORE

THE SELECT COMMITTEE ON SCIENCE AND TECHNOLOGY

(SUB-COMMITTEE II REGULATION OF THE UK BIOTECHNOLOGY INDUSTRY AND GLOBAL COMPETITIVENESS)

Thursday 22 April 1993

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THURSDAY 22 APRIL 1993

Present:

Flowers, L.	Renwick, L.
Gregson, L.	Soulsby of Swaffham Prior, L.
Hilton of Eggardon, B	Wade of Chorlton, L.
Howie of Troon, L. (Chairman)	Walton of Detchant, L.
Perry of Walton, L.	Whaddon, L.
Platt of Writtle, B.	

Memoranda by Hoechst UK Ltd and Hoechst AG, Frankfurt are printed separately

Examination of witnesses

Dr D Brauer, Public Affairs and Political Relations Officer, Hoechst AG, Frankfurt, Dr C Macdonald, Head of Research, Hoechst UK Ltd, and Dr W McDowell, Technical Director (Corporate Office), Hoechst UK Ltd, called in and examined.

Chairman

347. Good morning, gentlemen. Thank you very much for helping by changing the order of play. Would you care to introduce yourselves and perhaps tell us something about the background attitude which you have towards this matter?

(*Dr Macdonald*) My name is Dr Cameron Macdonald. Until one month ago I was Head of Hoechst UK's research and development group, but for the last month I have moved to our Head Office to take responsibility for marketing activities in the United Kingdom. I do not have a personal interest in biotechnology but clearly as head of the research group I was very concerned about biotechnology and any legislation pertaining to it with regard to future developments for my company.

(*Dr McDowell*) I am Dr William McDowell. I am the Technical Director of the Corporate Office. My interest as the Technical Director for all of our activities in the United Kingdom is clearly anything to do with legislation that affects our investments here, since I am responsible for the group investments and acquisition. I have been a member of the CIA taskforce dealing with the biotechnology regulations since its inception and I am now a member of the CIA strategy group for biotechnology which is chaired by the Vice President of the CIA.

348. CIA being the Chemical Industry Association?

(*Dr McDowell*) And not being the Central Intelligence Agency. My interest is ongoing in biotechnology as a member of that strategy group.

(*Dr Brauer*) I am Dr Dieter Brauer from Hoechst in Germany. My basic education is chemistry and molecular biology. I was several years at various universities, including Glasgow University, and joined Hoechst the chemical company in Germany in 1982. I worked as a molecular biologist in the pharmaceutical division and then I worked for another year in the United States. I then continued my work in the plant biotechnology division in Hoechst. In 1989 I joined the public corporate affairs group and in this position I was involved in all the hearings of the Germany Bundestag and I represented Hoechst as a technical expert. I am a scientist advisor to the Germany Health Ministry as well as on certain issues with the European Commission.

349. Thank you. Dr Macdonald sent us an interesting paper and I notice in the answer to question 8 you say that there is concern that some of the European legislation is over-restrictive, bureaucratic and inflexible, by which I assume you do not like it very much. I wonder if you could tell us what your principal objections to the legislation are?

(*Dr Macdonald*) I think my concern is based on my perception on how things may operate and this is partly based on our experience in Germany. I should say that our experience to date within the United Kingdom has been quite favourable and as a company we really have had no particular problems with existing European legislation, both in terms of product assessment and in assessment of risk within any process. Our concern is related entirely to how the EC Directives 219 and 220 may be implemented within the United Kingdom and, more generally, within Europe.

(*Dr McDowell*) We do actually use GMOs in our vaccine production in Milton Keynes and that is under an existing piece of EC legislation 87/22. We have had no problems with that at all. The Danes have always asked for further information when we submit, but we have lived very happily with that. We do not really have, as Dr Macdonald said, any experience with the current legislation since it has only been in force since 1 February. I would endorse everything he says and if indeed the United Kingdom implements this legislation, as they do in Germany, to make them the only two players on this two-party level field, then I feel that the United Kingdom will be equally disadvantaged to Germany against the other EC States which are long on talk and short on delivery and, in any event, the EC would itself be disadvantaged through the additional bureaucracy, double laws, multiple departments of Government which would be responsible for the actual licensing of the end product effectively and we would be seriously disadvantaged verses the United States and Japan.

350. Yours is a very big and important company and I rather imagine that when you speak people tend to listen to you from time to time. How much of an input have you been able to make into the preparation of these regulations a few years back and

[Chairman *contd.*]

to what extent are you putting something into the current discussions on revising the regulations?

(*Dr Brauer*) Hoechst has been involved with molecular biology and its applications since approximately 1980. Since then we have been engaged in research and development and also in production, at least we tried to get production facilities running. As Hoechst itself we were involved with advising the German Government, we were involved through the European Chemical Federation in the making of the Directives. This has a long extended history which actually started back in 1978. If I may, I would like to hand over to this Sub-Committee a text which I wrote a year ago, approximately, which covers a little bit of the history of these Directives and the unfortunate situation was that despite all the advice given from universities and companies the key parts of the EC Directives which are responsible for the disadvantages we have in Europe compared to the US or Japan have not been removed but stayed in these Directives. The problems that we have now in Germany with the gene law which has to be amended only after one and a half years of being in existence just reflects the situation and I must say that the European Commission has never shown any kind of consultation approach or transparency on the making of these Directives, on how one could actually comment on it and how these comments eventually could have been written in.

(*Dr McDowell*) I can endorse that completely from the United Kingdom point of view because all our submissions through the industry association failed to move the Commission.

Lord Flowers

351. Could I just ask, my Lord Chairman, whether these criticisms are criticisms just of the biotechnology regulatory system or do they apply to other regulatory systems under which you have to operate in any case?

(*Dr Brauer*) To my experience there was a very specific situation concerning molecular biology. There was a shift in the European Commission concerning the responsibilities from DG XII dealing with research issues and to DG III for economic affairs. Those two were responsible in the early eighties for drafting the first EC Directive guaranteeing some kind of overview more or less directed towards the handling of pathogenic organisms. Thereby for unknown reasons to us there was a shift of responsibility in the European Commission DG XI dealing with environmental affairs. It is clear in our view that the experience which had been accumulated and had helped agricultural agencies for 50 or 80 years in Germany as a European Member State is still not available to the environmental agencies. They have other tasks to do and they have a completely different understanding of what bio-chemistry and molecular biology is about and what the properties of micro-organisms are and what the difference is between non pathogenic and pathogenic organisms. This is somehow reflected in the EC Directives because they are based on a wrong scientific bases. We do not have recognised similar problems with other issues, whether it is transport of any kind of goods or whether it is the handling of chemicals, where there are actual consulting processes that one gets involved in a more or less official way on the developing EC Directives or whatever.

352. You are saying that they simply do not call for advice from appropriately qualified scientists?

(*Dr Brauer*) That is absolutely correct. I heard that myself in a meeting with the European Commissioner's administrators where they stated that they cannot consult us in an official way because for any kind of draft being prepared they would first need to discuss it with the national experts of the Member States and after the Members States' experts have given their opinions then these drafts are modified accordingly and after these drafts are modified accordingly there is no place for any comments by industry or universities in order to bring in additional modifications because they again have to go back to the national experts so there is no consultation process on these issues.

353. But the national experts come from universities or industry presumably?

(*Dr Brauer*) I cannot say where the national experts of other countries come from. In the German case they are representatives of the German Health Ministry of the Federal Republic and it is a lawyer and a bio-chemist dealing with these issues in the expert commission of advisors.

Chairman

354. Your company operates in Germany and in the United Kingdom and presumably elsewhere as well but when you are dealing with the national experts you presumably deal with the German ones and the United Kingdom ones. Do you find the same criticism can be levelled at each group?

(*Dr McDowell*) We have no experience of dealing with any of the ministries with these new regulations since they have only just come into effect. In fact, we are planning a meeting on how to tackle this. The products that we do produce using GMOs are produced in a batch process and we have actually finished that production. It is a nine-month cycle to produce one of these multi-component vaccines. So we had not needed to tackle this problem until just now.

(*Dr Brauer*) I think it is very difficult to compare the current situation to the previous one. As long as the former United Kingdom system of overview was in place, which was very similar to the German gene guidelines, which are again very similar to the NIH guidelines of the United States, you had comparable situations. Now the EC Directives have to be transferred into national law, they have to interface with other laws like the emission law and the drug approval law etc etc. There is a big problem with implementing the Directives into the German system because for the Contained Use Directive there has to be a competent authority in order to execute a review of other things. In the German constitution we have a division of responsibility at a federal and state level so the construction of buildings is naturally a matter dealt with at state level. The problem was, where does this competent authority actually fit in because the

[Chairman *contd.*]

building of research laboratories or production plants is a state responsibility. This construction authority now has to review to a certain extent experiments which may fall into safety categories, one, two, three or four in the German law but there is simply no expertise at state level in respect to biotechnology or molecular biology. Therefore these competent authorities have to consult a competent federal DNA advisory committee for all classified safety levels II, III or IV. This is a very lengthy process and this is why our experience in comparison to the United States or Japan shows that we have a very disadvantaged position.

Lord Walton of Detchant

355. Can I just ask, are you informed as to who the national experts are in the individual Member States and are you in a position to make submissions directly to them or must they go through the Commission?

(*Dr Macdonald*) I think it depends very much on the product you are talking about. You must remember biotechnology is not a single industry.

356. I appreciate that.

(*Dr Macdonald*) For some types of products we may have to deal with a national body and at other times, for example, with pharmaceuticals, we will deal with a European body.

357. You mean experts consulted in relation to the Directives?

(*Dr Macdonald*) I think the point I was trying to make in a round about way is that we are dealing with a whole range of different industries and the relationships we have with different bodies will be entirely different according to that industry.

Lord Renwick

358. In comparison with Europe and you say America and Japan, is it that they have greater scientific expertise or that they attract the right people or the regulations attract the right people?

(*Dr Brauer*) On this issue I visited the United States for two weeks with a colleague from Bayer Chemical Company in Germany and I returned 10 days ago. We inspected what it means in the United States to construct a research facility and what it means for a head of research in administrative terms? What is the time necessary in order to start an experiment etc? There turned out to be major differences. For setting up research facilities etc you only have to consult the local construction authorities. For the review process of research on small scale or large scale also concerning production facilities, you consult with an institutional local bio-safety committee. There is nothing like the competent authority as specified by the European Commission. You can start new projects after review within one to three days whereas the EC Directive states you may start work after two months, for example. So there is a difference between one to three days and two months here in Europe. In Japan you have a situation that resembles the United States. For facilities there is a clear and direct division between building and setting up a facility and the review process which is orientated towards the project. If a drug is to be approved there is also the FDA—the Food and Drug Administration—which looks at safety in the sense of the performance of the product in order to have these properties guaranteed. They also look into the facility itself, and, if it is built and constructed properly so you just have one approval in comparison to what happened in Europe. It is more flexible and much easier.

359. Your recommendation would be that Europe adopted a similar form of regulatory process but it seems a long way away.

(*Dr Brauer*) Absolutely. For the big companies I think it is clear that they can somehow choose where to invest and where to develop a certain product or to produce it. We are talking about bio-technology products and we are not talking about thousands of tons of chemicals per year but of high value products that can be shifted easily. In this respect one always has to consider the time it takes until you have a certain facility installed, in place, and how smoothly you can run it. Concerning the safety record of the United States system there have never been any kind of complaints. I think, even though it may be a long way off, it should be feasible to have something like this in Europe.

360. May I follow on by asking, is there not an association through which you can—not Hoechst yourself but as the whole industry group—talk to the potential Commission regulators?

(*Dr Brauer*) I am afraid this is not really possible because we have to go through the national Governments and this we do. As I mentioned before, the amendment of the German Gene Law after a hearing in February last year made it evident what the problems were and we have now come to a point where it is recognised, I think, by the Federal Government that certain changes in the gene law which would make sense are just not possible because there are the EC Directives in place. To my knowledge the Federal Government has already approached the Commission and mentioned that they are in favour of making sensible and reasonable changes to the EC system. I think this will take a long time and it needs support from other Member State Governments. As a company or, let us say, an industry organisation itself, it is difficult to engage in this process directly with the Commission.

(*Dr Macdonald*) I would like to make a very general comment because there is perhaps an underlying problem and that is the way that biotechnology is viewed in Europe in comparison with America and Japan. America and Japan do not consider there is anything particularly unique about biotechnology or gene modification. It is just part of a process and can be viewed in a similar way to any other industrial/production process on any product. They do not define biotechnology by a separate set of rules.

(*Dr McDowell*) My Lord, to give a crude analogy that may please my Lord, Lord Flowers: they treated biotechnology as they treated radio activity, by definition it is dangerous, and this simply is not true. Radio active substances have an inherent hazard and, therefore, it is quite clear that there are always risks associated with them. Biotechnology *per se* does not have an inherent hazard. Indeed, very often a genetically-manipulated strain will be less hazardous

[Lord Renwick *contd.*]

than a natural one; such a case we have in our particular vaccines in Milton Keynes.

Lord Flowers] I have a natural sympathy with what you say. May I persist on one point? If you were not consulted by the Commission, even informally on this issue—it seems odd to me if you were not—what steps are you taking to make sure that next time there is a Directive in your area of business you will be consulted?

Lord Walton of Detchant

361. Can I just follow that up by asking, in the United Kingdom, which Government Department in the field in which you are particularly concerned is the competent authority for appointing these experts?

(*Dr Brauer*) In Germany the experts' appointment is a matter for the Ministry which is responsible and the Federal Governments appoint a certain Ministry in Germany. It was the Health Ministry which had the lead concerning biotechnology. Then it is up to the internal administration to appoint those persons who represent the Federal Government or the Health Ministry as national experts with the European Commission. The problem we are facing is that industry is not approached directly on these issues by DG XI but only through the national experts who then in practical terms have the problem that once they get drafts or are asked for comments there are only ten days or something like that left in order to comment. To get within ten days the experts in industry and universities and other research organisations to bond, to prepare for this meeting, to bring down in writing opinions, has shown within the last few years that the suggested time-frame is too short and this cannot be done. The other question of consultancy has to be addressed I think in a very specific way. I have no answers currently how this could be changed with the European Commission. I know that the Federal Government of Germany has approached and has tried to get different procedures for consultancy but so far it has not been successful.

Lord Flowers

362. I am sorry to go on about this but I understand of course that the bureaucratic system which I suppose is forced upon Brussels to a certain extent does tend to lead to the situation you have just described. On the other hand, most of my experience of the Commission has been that in an informal way they consult quite a way ahead in time.

(*Dr Brauer*) That is our experience on the issue we are talking about. If it has to do, let us say, with pharmaceuticals and the certificate for extended patent protection—I do not know what the correct term is— There have been extensive consultations with DG III as to whether it is a research issue which was of the IRDAC, the round table advisory committee which I am also a member of. There have been many attempts and many contexts but concerning molecular biology and biotechnology DG XIs, this has not been in place, maybe because there was this shift in responsibility a couple of years ago and there have been no established connections.

Baroness Platt of Writtle

363. My Lord Chairman, Dr Brauer has described what happens in Germany and which departments are involved. What happens in Britain?

(*Dr McDowell*) In the United Kingdom the situation was until 1 February this year in many ways very similar to the situation in Germany. I have a flow chart here which describes how you actually get approval with a critical path analysis from having an idea to put up a project involving genetically-manipulated organisms to actually manufacturing it. The final licence would come from the Medicines' Control Agency which is a Department of Health sponsored body, but you would en route to that go through many other departments of state. You would start at the local planning authority, you would involve the Health and Safety Executive, you would involve the National Rivers Authority, you would involve HMIP, the fire brigade, the CIMAH regulations, the IPC regulations, the Medicines' Control Agency and, laterally, of course, the Department of the Environment.

Lord Gregson

364. Chairman, I think the original question was seeking who you would approach if you wanted to influence the Commission. There is a Government party nominated, as far as I know, for that purpose.

(*Dr McDowell*) I understand the responsible department will be the DoE for two of them, 219 and 220.

365. I thought the Government Chemist was actually the nominated figure in Government for dealing with biotechnology?

(*Dr McDowell*) We make all our submissions through our trade association, I generally through the CIA, my colleague through the ABPI and other colleagues through the BAA and who the trade associations finally deal with, to my knowledge they deal with the HSE directly and the DoE directly, people like Peter Corcoran.

Lord Flowers

366. Do you feel inhibited by approaching, let us say, the Government chief chemist?

(*Dr McDowell*) Personally, I would not feel the least inhibited in doing so. I just do not see that there is a vehicle for making that formal approach; informally perhaps.

Lord Soulsby of Swaffham Prior

367. I was just wondering whether you compared the regulations in the US and Japan with those in Europe, but the regulations in the US, to my knowledge at least, involve the evolutionary process when ten or fifteen years ago they were very strict indeed and now they are much more appropriate and they have been modified by pragmatism and realism in a way because of the massive development of biotechnology in the USA that with the very restrictive educations that the whole thing would grind to a halt in a way. Do you not think in the European sphere that the same might happen, that you are going to have to use a lot of pressure, but it is

[Lord Soulsby of Swaffham Prior *contd.*]

an evolutionary process you have got to go through and not one that is going to be changed overnight? Obviously biotechnology is going to grow very substantially and it is a question of pragmatism to let it grow and realism too because people realise that the danger is not there that they foresaw.

(*Dr Macdonald*) It would certainly be very nice if it was to go through some sort of evolutionary process where a better understanding of biotechnology was to develop, but we are dealing with the situation as it presently is and there are genuine concerns about these new EC Directives and how they are going to be applied in Europe. Investments are being made now—and I speak as a member of the United Kingdom scientific community and not only as a member of my company—and we want to make sure that the United Kingdom is a major player in the future development of biotechnology. I think that is a fundamental need of this country and we are in danger of missing opportunities unless we take the right steps now. I do not think we can afford to wait.

(*Dr Brauer*) I fully agree with what he said, that the US system has developed or evolved from a long history of working with different organisms. In the United States I think very appropriately completely harmless organisms are exempted from regulatory overview. We have in the EC Directives the so called "type I" organisms which resembles them but they are not exempted from the EC system. Just to make that very clear industry and universities are not asking to have no regulations. There must be regulations. There must be safeguards in handling pathogenic organisms. The more pathogenic the organism is the more precautions have to be taken. That includes bio-technology but there is no need for direct regulations for completely harmless organisms, that is in micro-organisms or plants. That has not been recognised by the European Commission unfortunately. This is done in the United States, and the expertise that was developed was at the Food and Drug Administration concerning food and drugs and it is being used in a very appropriate way and everything to do with plants is very appropriately handled by the United States Department of Agriculture whereas here it is the Environmental Agency which is a nonsense.

Lord Wade of Chorlton

368. Listening to a number of your arguments you are putting, on the one hand clearly biotechnology is becoming in the public perception something of concern. But you say on the other hand that you find it difficult to put your point of view to the necessary agencies to listen to the benefits. Clearly from what you are suggesting the agencies are moving towards a state of caution rather than a state of reality. Clearly those who are not in favour of biotechnology seem to be able to get their point of view over to the regulatory authority better than you do, Why and what do we need to do about it?

(*Dr Macdonald*) I guess this is a matter of public perception and clearly those against biotechnology do attract much more press attention. I think we as an industry we as members of the scientific community have not necessarily put forward a very strong campaign. "Why" I think is something which needs to be readdressed. I do not think it is just biotechnology. I think science itself is under a bit of a cloud and biotechnology is certainly caught up in this. I think there are certain groups who see even the industrial development of gene technology as the thin end of the wedge and there is very genuine concern that they will put in place any steps they can to prevent the development of this technology. This is reality and it is something we have to be aware of. It is a point of view that will be shared by many people but I think we have got to take a pragmatic, sensible and realistic approach to biotechnology's importance in terms of science and the future investment in the well-being of this country and those who live within it.

Lord Whaddon

369. I can appreciate the frustration that you, Dr Brauer, have in Germany in particular. I have the impression that "Green" groups have had a tremendous impact Germany, far greater than the United Kingdom. Do you find that is so?

(*Dr Brauer*) Yes, sure. I would fully agree with that. It is certainly true there is the existence of the Green political party but many of those ideas have actually been moved into public, into the media and there has developed simultaneously a big distance between science and particularly one tends to ignore the world-wide expertise. A good example is the current negotiations on novel foods, where you have recombinant tomatoes on the market where many people in Germany believe, as the media claims, there are some kinds of hazards. It is interesting that there was a book published back in 1992 where all the scientific data on these recombinant tomatoes, which was produced in the United States and which is an important comment on the market, and has put together all the data concerning the analytical analysis surrounding the issues and inspecting the potentially hazardous components that might be in tomatoes. All this is put down in a book that is publicly available but it is ignored in Europe that this scientific data is available. It seems the European Commission tends to wait until everything is repeated. We are re-inventing the wheel in making a German analysis of recombinant tomatoes more accurate than the American one. I personally have my doubts about this.

370. I know Poland quite well and I was asking therefore what their attitude was and their attitude was complete revulsion. They took the religious view that one must not meddle with nature. I wonder if there is something of the same in Germany?

(*Dr Brauer*) That is very much the case. Even with the environmental organisations there was a distinct difference back in 1986 when there was a general agreement in the largest environmental group that they opposed any kind of application of molecular biology no matter what it was, including health or medical research. Now it was changed in 1989 when they modified this view by stating that they accepted medical research, the production of pharmaceuticals and other things. They still reject anything like deliberate release of recombinant organisms, which I think is fair because it is an environmental organisation and otherwise they would lose their

[Lord Whaddon *contd.*]

members! This more differentiated view in particular was never reported in the press and media. The first statement rejecting everything was published everywhere. After they had modified this view not that recently this was no longer reported and I think the public and many politicians are still not aware that they have changed their views. Concerning the religious point we currently have certain people are putting down their (?) on those spots where we have certain authorisation to conduct field-testing this year. So they have been planting their (?) there to hinder the planting of these recombinant plants or seeds.

Lord Flowers

371. My Lord Chairman, it is quite understandable that environmental considerations come first in some countries, Germany certainly and to some extent this country as well but in this country we have a Department of Trade and Industry whose job it is to try and help industry where it can. It does at the present time have a deregulation taskforce. Have you made representations to them?

(*Dr McDowell*) My Lord, if I may answer that. Yes we have a Hoechst UK Board Member on the CIA team that is looking into the Heseltine initiative on deregulation. I myself have given an interview to one of the taskforce and we have actually raised the issue of these three parallel Biotechnology Directives as a special issue within our discussion with the deregulation taskforce.

372. With what result?

(*Dr McDowell*) We do not know. I only gave my interview 10 days ago.

Chairman

373. You have seemed to me to be highly critical of the regulations and not only that but about the means by which they are arrived. However, I see in the letter from the German office, I think this is your letter, Dr Brauer?

(*Dr Brauer*) Yes.

374. In the first comment you make under point one you say that all major political parties in the Bundestag have expressed their support in simplifying these regulations. So that suggests the picture is not quite as gloomy as you have painted it this morning.

(*Dr Brauer*) There was a hearing last February where research organisations and the universities and industry explained what the problems are. Now there were political protests which ended in debate in the Bundestag last November and both groups in parliament had presented certain key points which are to be amended in the gene law. The coalition governmental parties had only minor differences to what the Social Democrats actually wanted to have changed. After the voting certain key points have now been put into a draft in order to change the German Gene Law. The decision was to make it within the framework of the EC Directives. This draft has been published meanwhile and has already been commented on by chemical industries and others. Whether this comes into effect is quite a different issue because it has to go through the presentation of states and all the other ministries have to give their input. So whether there are significant changes to be expected by the end of this year/beginning of next year is, we understand, very questionable.

Lord Walton of Detchant] Do you think that it is possible the English law can be drafted in such a way as to take account of the EC regulations but be very much more user friendly than that which has been passed in Germany?

Chairman

375. I think we will make that the British law!

(*Dr McDowell*) There are no English present, I am sorry. We would like to hope that that would be the case. We do not know how to go about influencing that. We are very pleased, of course, that the third Directive, the Protection of Workers, will now be implemented under the COSHH regulations. It will be mopped up in an existing regulation. What we do not understand, of course, is why the Contained Use Directive is in any way necessary because we have under our existing gene regulations quite sufficient regulations to deal with genetically-manipulated organisms. I come back to the point, a pathogen is a pathogen is a pathogen and it does not matter whether you produce it by genetically manipulating something or not. You have always had strict regulations as to how you contain that.

(*Dr Brauer*) If I may add to this, there are two EC Directives dealing with this issue. One is very appropriate, namely the Protection of Workers from Biological Agents. This Directive distinguishes four different risk groups and removes one because there are no risks. I think this is very appropriate. Unfortunately, the EC Directive on Contained Use from Modified Organisms does not distinguish four groups but distinguishes two groups, Group I and Group II, where Group II comprises all pathogenic organisms, and Group I is not exempted. The provisions given by both Directives and the annexes concerning the construction and containment details of facilities differ and this is something which actually one cannot really follow, and one does not understand why there is one Directive dealing with pathogenic, often dangerous organisms, and why there are different rules which apply for laboratory facilities in the other Directives than there are for the GMO Directives. It has to be sorted out.

Lord Renwick

376. My Lord Chairman, I am conscious of time and the fact that we have kept on regulation, but Dr Macdonald in his submission mentioned intellectual property rights. I do not know whether intellectual property rights are governed by regulations, but I wonder if Dr Macdonald would like to tell us in his experience how his company has been prohibited from going down a particular course of research and development because other companies have the intellectual property rights or whatever?

(*Dr Macdonald*) I am no expert in this particular field, but the discussions I have listened to have indicated to me that there is still great uncertainty about what can be protected. I think this is an

[Lord Renwick *contd.*]

inevitable consequence of this type of technology, whether it be the protection of a process or protection of a product, but it is something which I think there needs to be a gathering of minds on across the international community. This goes far beyond the United Kingdom. We ourselves have been adversely affected by competing patent claims from other companies. We only found this out having made a major investment and clearly we would rather the ground rules were established very early in the process of investing in this sort of technology so that we actually know where we can go, what we can do and what our rights are, I think we need to review both the European patent laws and international patent laws for biotechnology products and try to build them into the existing legislature that covers conventional chemical entities. This would be my recommendation.

Lord Renwick] It seems, my Lord Chairman, we are going to have the problem of vertical or horizontal patenting in these regulations.

Chairman

377. I think we know where they stand on the horizontal/vertical thing. Still on patenting, we put through an Act in this country in 1988, the Copyright, Design and Patent Act; you are telling us that does not go far enough?

(*Dr Macdonald*) Again, I do not have personal experience of this and it would be unfair for me to make too detailed a comment. My understanding is that there is still considerable confusion. We are not yet sure of how best to protect our intellectual property rights.

Lord Walton of Detchant

378. There is a related issue on the other side of the fence. Obviously you are concerned with commercial success as a very successful commercial company but the field of biotechnology is now so huge one wonders whether there is any gathering of minds between countries across the world relating to the specific fields upon which individual companies will concentrate in order to avoid unnecessary duplication of effort in this very wide area.

(*Dr McDowell*) My Lord, the patent issue is an issue which is always referred to at the CIA's strategy group. It seems that the OECD cannot really come to a conclusion on this issue. Take the farmers' rights issue, if he takes a genetically-manipulated potato seed and buys it once, does he forever have to pay a royalty when he uses his own produce again and again? The whole biotechnology area is a bit of a minefield.

(*Dr Macdonald*) One further point of concern I have about the patent law is whether anyone has the right to patent an actual gene. I would differentiate this from technological development within biotechnology where a new gene is created.

(*Dr Brauer*) On the European level, I want to say that the senior advisory in biotechnology, which consists of 30 different companies also has addressed the question of patenting and intellectual property protection in the field of biotechnology and is continuing to do so. The key point I think we made is not the question whether it should be allowed or not be allowed to patent life, but whether there is some kind of protection for investment for developing certain products, which might be therapeutic products or food additives. There is certainly much money involved in the development process which may take ten to 12 years and cost, in the case of pharmaceuticals, beyond DM100 million or even more. Unless there is a certain protection you have for the development of such a product and for the marketing, then these products will not be developed and, as was announced a couple of days ago, Hoechst in Germany joined into an agreement with another 15 companies—just to give an example—to develop and screen existing chemical compounds whether they are active in defeating the HIV virus, simply because many of these pharmaceuticals already approved have lost their patent protection. When you accidentally find such a compound which might be active and help cure or delay the disease AIDS, then the development of this product would cost, with all the clinical studies to be conducted etc etc, something like DM100 million. Because the compound itself is no longer protected, any other company capable of producing this compound could refer to our clinical data and then market this product for a much lesser price. We cannot just do this ourselves therefore many companies have put together their efforts and then eventually it can be financed but not by an individual company. If something like this happens to the development of new modern products from biotechnology, then I would say in Europe we can forget about developing such products.

Chairman] We have come to the end of our time but there was one more question?

Lord Soulsby of Swaffham Prior

379. It was this long-term concern that you have expressed in your submission about the infrastructure research training and I am just wondering if you have any brief comments to make on that, what suggestions you have to modify this to the benefit of the biotechnological industries, if one can call them that?

(*Dr Brauer*) Do you mean the EC Directives?

380. No, not Directives, but in terms of research training in universities and in biotechnology.

(*Dr Brauer*) Well, for the German educational system and university system we have certain differences to the United Kingdom system or to France. I am not sure actually how this could be approached. Certainly the question, if you mean this, of time-frames or waiting periods until certain experiments may be started has to be changed. As I said before, the adopting of some of these practices of the United States would help a lot.

(*Dr Macdonald*) One final point on that. The key to having a strong straining influence is to have a thriving biotechnology industry and without that investment, both by industry and by government into universities and other educational establishments, we will not have that scientific base.

Chairman

381. Thank you very much. At a later date when you have seen the transcript of your evidence you may wish to amplify certain parts of it or even modify certain parts. I think, Dr Brauer, you are going to submit a paper?

(*Dr Brauer*) Yes.

382. Thank you very much. It would be nice, Dr McDowell, if we could have that flow chart of yours.

(*Dr McDowell*) Yes. It is using a French system, I am afraid, MPN for critical path, but it shows the existing system and how you can get from an idea to production in 100 weeks.

383. If we could have a copy of that?

(*Dr McDowell*) By all means. There is also a sample of how the old system worked through the Medicines' Commission.

Chairman] Thank you very much.

Memorandum by SmithKline Beecham is printed separately

Examination of witnesses

DR G POSTE, Chairman, R&D, DR J M DEWDNEY, Director and Vice President Biotechnology (Europe) and MR T SAVIDGE, Director, Biotechnology Development Worldwide Technical Operations, SmithKline Beecham, called in and examined.

Chairman

384. Good morning. We have met Dr Dewdney before I remember.

(*Dr Dewdney*) Yes.

385. Some of us have had at any rate. She very kindly gave some advice to Lord Perry a few weeks ago on a different matter. Thank you very much for that. Would you introduce yourselves for the record and then we will proceed from there.

(*Dr Poste*) My Lord Chairman, my name is Dr George Poste and I am Chief of Research and Development for Smithkline Beecham which is an organisation of approximately 5,000 scientists and technicians who are located in 18 R&D sites around the world with approximately 40 per cent of our manpower in the United Kingdom, 40 per cent in the United States and 20 per cent in the remainder of the world.

(*Dr Dewdney*) I am Dr Janet Dewdney and I am responsible for research and development in biotechnology in Europe.

(*Mr Savidge*) My name is Tom Savidge and I am responsible for the development of biotechnology processes within our world-wide manufacturing organisation. I am based at Worthing on the south coast and I am a microbiologist by profession.

386. Thank you. Now Dr Dewdney submitted a very interesting paper to us. I am looking at page seven and the answer to the question eight . The paper refers to Directives 219 and 220. It goes on to talk about the extremely poor quality of these Directives and the confusion and bewildering complexity and the alarm, I think, that these Directives might be applied horizontally across all sectors. Now are the Directives really as bad as all that or how bad are they?

(*Dr Dewdney*) My Lord Chairman, there are two ways of answering that. Given the need for the United Kingdom government to introduce legislation based on the Directives I think they have done a pretty good job. They have developed a middle-of-the-road pragmatic view which we can certainly live with within the framework of having to introduce legislation from the EC Directives and I am in this respect supportive of the United Kingdom government. But, I believe that both the framing of the Directives from the EC and more importantly their strategic intent was totally wrong. So I think we are trying to make something good out of something which was strategically incorrect in the first place. My reason for saying they were strategically incorrect is that they are discriminating against biotechnology and in particular against GMOs. There is an assumption in the Directives and therefore coming through to all legislations that GMOs are *per se* inherently hazardous. You have heard from the last witnesses that this really is not so. That is really why I am making these comments.

387. You do say something nice about the United Kingdom further down in that same entry. You go on to say there are still a number of detailed matters which need clarification. I was wondering whether you could tell us what these are unless they are too scientific for us to understand.

(*Dr Dewdney*) I can answer fairly generally with one or two specifics. You heard just now of how much discussion it was possible to have during the framing both of the legislation and of the Directives. I would agree with the last speaker. There seems to have been no opportunity for strategic input but we have had quite a lot of input operationally during the draft stages. So the first draft was full of things which would have been very difficult indeed to live with in a legislative framework and they have been altered with subsequent drafts of the concerns that remain I think some of them are detail. I very much welcome the change in the self-cloning definition but there are still some aspects there. There is one I know I am told I should not worry about but I do and that is the discrimination on the basis of size of operation.

388. This is the 10 litre rule?

(*Dr Dewdney*) Yes, 10 litres. I think it is irrelevant to risk. What matters in risk assessment is containment. You can have as much risk with 10 litres on the bench with a sloppy worker and leaky valves as with 3,000 litres in a well-contained and well set up arrangement. People say, "Don't worry, the HSE will take a lenient view of that 10 litres which was meant anyway to be an approximation." I do not think that is appropriate in legislation. Is 100 litres "about 10 litres"? Is 3,000? This is a very important point, sir, because if we put a constraint upon the scale of working within these limits we are going to be highly uncompetitive in research. I am not talking only about manufacture. I am talking about research

[Chairman *contd.*]

initiatives also. It is important that this scale of operation issue is clarified. I do not think size *per se* is a risk hazard so it should not be in the legislation for Group I organisms.

Chairman

389. I have given a little amount of fairly superficial thought to the idea of 10 litres and it struck me that 10 litres is about the size of a case of whisky which is not very much, let me tell you!

(*Mr Savidge*) Could I just add to that. I think the description of size should be based firmly upon operational standards relative to the risks as determined by risk assessment and that is not the situation as it exists at the present time.

Lord Renwick

390. Could I, my Lord Chairman, ask Dr Dewdney about risks. We are talking about GMOs being inherently hazardous but you are saying they are not. We are talking about regulations trying to cover where you in your company under your own procedures are desperate to get on the right side of the hazardous problems. It would help me enormously and maybe my colleagues if you could define what possible risk that regulations in the United Kingdom or in Europe might prevent, which the Americans or the Japanese might not prevent or just generally what is the worst case scenario? Thalidomide is within my knowledge as a problem for your industry but maybe that was not genetic. I do not know whether that was a genetically-modified organism—I am sure it was not—but it was something which the regulations of the time in the distribution, probably right at the market end did not prevent. Could you talk on these levels as to what possible risks there might be?

(*Dr Poste*) The question obviously embraces a very broad spectrum of risk but I think that one should look at where natural genetic re-combination is occurring in the environment when, for example, an organism moves from one species to another. The most virulent outbreaks of influenza represent genetic reshuffling between genes moving between influenza strains that affect different species. There is clearly a credible school of thought that argues that much of the virulence of HIV reflects the movement of an agent which had previously been relatively innocuous in the context of its simian host that once transferred into a different host displays entirely different virulence. I think the broader issue comes back to the one that my colleagues have already re-enforced and that is the fact that there is always a theoretical risk which must be conceded and certain manipulations may create unknown risks, no matter how all embracing the regulations may seem to be. I think the issue, with respect, Sir, that has caused me and many of my colleagues in the industry concern has been that there is almost the implication that the Americans are less conscious of risk. This is one issue, on which after debating with great regularity with the FDA, I can re-assure you. They exhibit great caution. I think that your worse case scenario is the fact that a worse case could occur theoretically under any circumstances. Most important, we do not believe that that is in any way associated with a risk unique to biotechnology. I have mentioned some of the naturally occurring risks and other techniques which have been used in research laboratories for years, in terms of mutagenesis that may in fact be producing far more profound change in the genetic make-up of organisms that are not subject to any form of regulation whatsoever.

(*Dr Dewdney*) Could I, Sir, come back on the question, too and re-enforce that. My concern comes back to this size issue. We have Group I organisms—and I apologise that there in my document I call them Type I—which are by definition non-hazardous. The regulation then says that if you put a non-hazardous organism into a larger scale, round about the ten litre scale and up, suddenly you need 60-days notification. Why? What can possibly be the scientific basis of such a regulation, and I am not playing with words or being contentious. This would put a severe restriction on what we personally do in our research and that is the basis of the argument that I am developing. The second point of your question is a very real one. Of course there will be risk and of course we take every precaution now, but risk is related to your ability for containment and worker protection and that legislation and control is in place. This includes GMP or GLP, whichever standard one is working to, and that is also in place. There does not need to be any extra protection because they happen to be, in this case, non-hazardous GMOs. It makes no scientific sense.

(*Dr Poste*) And not merely to pursue semantic purity because, as Dr Dewdney has emphasised, if something is judged to be hazardous and subject to the legislation based on this magical threshold of ten litres it will impact at the operational management level—not just in terms of formal compliance with the regulations—but in also requiring you to then accord a different status to the process internally, for example, if anything were to occur from a totally unrelated event but, nonetheless, within the contemporary framework of litigation, it could always be claimed because an individual was then working beyond the magical ten litre level that the injury or risk was dur to the process. You will have a lot of hidden accessary costs that will have to be added merely because of the false classification of the process as hazardous.

Lord Walton of Detchant

391. May I take up a point which is I think relevant. I think we are all satisfied that the containment regulations are satisfactory and effective but in your paper, Dr Dewdney, at the end you refer to the prospect of gene therapy now becoming a reality for the treatment of human disease. You mention potential public concern about the manipulation of the germ line, but I would have thought that manipulation of the human germ line is specifically precluded by the Human Fertilisation and Embryology Act. The other point that I wanted to raise is the one relating to the use of viral vectors to carry genes into human tissues. One of our witnesses in written evidence has said that, for instance, if you were to use an adeno virus and splice a gene product into it, you thereby, by cutting out some of its own DNA, will remove its pathogenicity.

[Lord Walton of Detchant *contd.*]

If that virus, nevertheless, having been inserted into the human subject subsequently came into contact with the comparable wild virus, then it might become pathogenic. Have you any comments upon how that can be prevented?

(*Dr Poste*) I am not sure I will immediately concede the legitimacy of the theoretical premise. I acknowledge at this stage no-one has a sensible procedure to contain that risk if it occurred. As you well understand, what is the nature of the genetic regulatory element that would have to be picked up to suddenly cause genetic reversion. That is then a complex issue in its own right. The second issue is, what is the tissue trophism of affinity of that particular virus? Therein lurks a problem which is even relevant to inadvertent germ cell line modification. If you have a pantropic vector which can affect all cells in the body, including spermatozoa and ova, then you have inadvertently created a vertical genetic modification. All of these permutations can be constructed as a theoretical degate and occupy us for many hours. Gene therapy *per se* is a deliberate genetic modification whether it be a monogenic or multigenic disorder of a single human being; it is indeed very different to the issues being debated here and poses a different set of questions which I am sure could occupy this Committee for many weeks on a future occasion.

Chairman

392. I hope not. There are side effects to regulations quite apart from the scientific aspects. On page ten of your paper, Dr Dewdney, you refer to the exploitation by British industry of research and so on, and you say that SB is currently exploring options for a manufacturing plant. You go on to say that in spite of a strong research base in the United Kingdom this plant is unlikely to be in Europe. Partially that may well be for strategic business and partly because of the regulatory regimes in Europe. Can you give us any idea to what extent the regulatory regime is a determinant in such a decision?

(*Dr Poste*) My Lord Chairman, if I may, I will respond to the extent that I am the individual charged with that decision and I think Dr Dewdney obviously prepared this document in consultation with me. It is not necessarily an overtly US centric position that I will adopt but this is one trend which we are seeing certainly in our own company and many others. You are correct in identifying the fact that it is a complex montage of strategic issues, taxation, the availability of skilled manpower and two additional factors that the Committee may wish to consider which is obviously the ease of technology transfer from R&D to manufacturing operations. When you are dealing with established technologies that, say, the pharmaceutical and the chemistry industries are well used to working with such as very small molecules produced by traditional chemical synthesis, you can have your R&D centre at a geographically remote location from your manufacturing facility. In biotechnology the skill base in manufacturing is sufficiently new and technically demanding that you need a close geographical proximity to the R&D operations to ensure a smooth transfer. That is a purely strategic factor. An element of any decision on location must be subjective and such judgements include overall perceptions of the regulatory climate and the national receptivity of high technology. (I apologise for the relative lack of specificity). This embraces regulatory attitudes and the level of support for the science base and the third, touched on in earlier discussions, how far the neo-Luddite lobby can be effective in mounting opposition to scientific and technological effort. I think all of those come into it. It is difficult to apply a specific weighting but regulations do certainly impose another hurdle onerous regulation implies that it is not a climate of suitable receptivity for investment in high-technology resources but it clearly goes well beyond regulation.

Lord Soulsby of Swaffham Prior

393. Are you satisfied that there is the science base in the United Kingdom or Europe to supply your needs?

(*Dr Poste*) No. That is something I can be absolutely unequivocal about. I believe there has been an unfortunate erosion of the science base in Britain over the past two decades. I think it has been an attitude of passive neglect rather than purposeful policy. Nevertheless the effect, not just within my own industry but in all aspects of society which depends upon the availability of a numerate and literate workforce is cause for concern.

394. What would be your proposals to alter that especially from the private industry point of view?

(*Dr Poste*) I think that the pharmaceutical industry clearly has received deserved recognition in the United Kingdom for its leading position in the high technology sector. Several elements are important starting with stable long-term funding of research and development. A highly sophisticated internal infrastructure which allows you to rapidly assimilate new technologies is also fundamental to success. This in turn, requires a substantial commitment to internal training and development to ensure that technological obsolescence does not overtake one's workforce. There is also the size of the reservoir of available talent. To date his has not been limiting but I think it is becoming increasingly problematic but it differs within different scientific disciplines. You cannot make it an all-embracing thing applicable to every scientific discipline.

Lord Renwick

395. I understand biotechnology accounts for 10 to 15 of the Framework Programmes applied for in the EC. Does your company take part in the Framework Programmes. Obviously it is competitive but you are saying that the science base in the United Kingdom and Europe obviously compares badly with the United States. Are you taking the Framework Programme into account?

(*Dr Dewdney*) Yes. I have to say that one has to be really committed to try to access any of the European-based funding research schemes. The input documentation is overwhelming. In addition to that we are very active in the COMETT scheme which is a European funded studentship so that students are trained within industry. We have one or

[Lord Renwick *contd.*]

two industrial students a year and this is a very valuable resource. So we are active in Europe and within the United Kingdom, in initiatives like Bridge and other DTI sponsored programmes.

(*Dr Poste*) I am not sure this is a reassurance but many of the comments I have just made as applying to the science base in the United Kingdom would also be relevant to the United States. This is a more general problem, reflecting the retreat from science as an attractive career opportunity. This has its origins all the way back to the secondary education curriculum and extends to the tertiay education curriculum. It is a problem that besets most of the G7 nations today, with the possible exception of Japan.

Lord Wade of Chorlton

396. But following on from what Dr Poste was saying earlier on the perception and how the industry has developed clearly the industry has gone ahead according to what many people in the Community can accept. You have got this position in the Community of what the industry can do and what people want it to do. Do you feel that is something that will resolve itself with time or do you believe it is of such a serious handicap to the industry and with the regulatory aspects that are now coming as a result of that attitude, that in fact something more positive has to be done to bring the Community much more up-to-date as to how things are developing. If something has to be done, do you see that as something that the industry needs to take a better grip of or is there is a role for government to play in order for it to be achieved?

(*Dr Poste*) Obviously there are multiple facets to that question. Firstly, I am not very optimistic that it will come to a quick resolution. I think this is an issue which transcends biotechnology and relates to the broader issue of how society perceives science and technology as perhaps creating problems of a magnitude that it does not know how to grapple with. as in the earlier discussion on this topic, in the Hoechst depostion there is an element of genetic modification that escalates covert fear of science and technology to a new level due to the moral, social, ethical, religious and cultural issues; these vary in different parts of the world. I do not think industry has been effective in the overall positioning of new technologies, biotechnology included, in response to public concern no matter how exaggerated public concern may be. Any perception of risk is real as far as the public is concerned and I think the industry must be more active in the public debate but I do not believe however, that industry alone can solve this. It requires a very balanced presentation of all elements of the risk benefit equation and its overall relationship to international competitiveness. The debate must involve all of the key consitutencies—industry, academia, government and the public.

397. What worries me is a number of issues which have been stated—clearly looking back science-led developments have made extra wealth within the world possible. Everyone has gained enormously from it. Now it seems that you are suggesting an attitude that is anti these scientific benefits. If that is so the downside on the future is enormous because we will not be able to develop activities which are going to be essential if you are going to have greater wealth and benefit for everybody. There is a very important issue here. At some stage you are taking it out of the biotechnology field and putting it into science generally and it is going to have a very serious downside on the future of societies if we cannot convince many people of the importance of future developments.

(*Dr Poste*) Very much so. I think that captures it very well. Again I am afraid my comment is not constructive in the sense of offering even a glimmer of a solution but it does go back to the overall level of basic scientific literacy in our society. I do not think that has to necessarily proficiency in writing complex equations on the back on an envelope rather where very few in society have any capacity to make even the most marginal assessment of the risk versus benefit we will face distortion of risk and the more cocooned society appears to become to risks the more sensitive it appears to become to risk derception no matter how remote. I think it would be a disservice to this Committee in merging public concern over biotechnology to overall concern about science and technology if I indicated that I do not have concerns about the fact that the valuable development of biotechnology within industry for the benefit of human health and quality of life might be compromised ahead of certain other technologies. The issue of gene therapy and gene mapping will have a much more confrontational perception as seen by the public. If you have an explosive growth of gene mapping repertoires over the next decade, in which all of us are revealed to have genetic codes that identify particular genetic disease predisposition markers, this will define a new category, the pre-symptomatic ill. The Americans with the Disabilities Act, for example, have gone some way towards trying to circumvent this issue as a criterion for discrimination in employment or insurability. This is also going to play a very important role in the future as you begin to address another very large issue which is the fact that technology is far outstripping the capacity of society to pay for health care. When you have an entirely new range of tests that can predict disease patterns and arrange for earlier intervention, yet also in certain cases lead to a decision to withhold therapy, then society will obviously be forced to debate very complex issues I consider that more challenges will emerge in the course of the 1990s.

Chairman

398. I would like to go back to the paper. I reflect that it is more than 30 years since I looked at a differential equation in anger, but I know exactly what you are talking about. From this paper I get the impression that you strongly favour what is called vertical regulation rather than horizontal. We were told some weeks ago by a witness from the Department of the Environment that the differentiation between horizontal and vertical is academic, the regulations are risk based. Is the difference academic or are we tilting at windmills here?

(*Dr Dewdney*) I can answer that. I do not think they are academic at all. I think they are very real and

[Chairman *contd.*]

your question that you posed before the meeting I think illustrates a very important point. First of all, you know my view that the regulation is not risk based. Even were it so, then I think this issue of horizontal and vertical legislation becomes a very important one within our industry, which is pharmaceuticals. We are used to being highly regulated. We are used to providing a great deal of evidence about the safety and quality of the products that we put forward. There is no additional benefit to be gained from an input of horizontal legislation with respect to GMOs. Our products have to safe, they have to be effective. The way they are manufactured, the process by which we reached them is irrelevant to that argument. They are safe or they are not safe and they are effective. Where horizontal legislation must play a part of course is in research and development. There is no other way of doing that and that, of course, is no different from everything we have been used to in the past. But the question raises a key secondary question, if I may, which will be answered differently by every industry involved in biotechnology for different reasons. In the pharmaceutical industry we have all the product legislation in place throughout the Medicines' Control Agency and I can see no justification whatever for going outside the agency control of that activity. In other industries there may be very different concerns, with transgenic plants, for example. There may very well be the need for some other type of control process there, but for the pharmaceutical industry I can see no place for horizontal legislation at the product legislation stage. I just cannot see that it adds anything other than creating several doors with different keys through which one must go. We have always argued strongly for a single door and a single key and that is the route that we must go for our product registration.

399. I think that is a really direct statement of your position with regard to the DOE's views. In the paper you go on to say later on that the US regime is more transparent than that that prevails in this country. Can you illustrate that by examples of some sort and perhaps tell us what the effect in money terms is? Is the transparency cheaper, so to speak?

(*Dr Dewdney*) Yes. I will answer the second part of penalties of the question first. It is not a question of experience *per se* but of the financial penalties of delay and uncertainty. Where the difference lies is that in the United States they have the same regulatory process whatever the micro-organism may be. There are no special regulations, so they have introduced their control of GMOs, within their existing legislation, so one has known for many years what that regulation is, what the control is and wherein lies the responsibility. A lot of the responsibility for the control is down to the operational level, in other words, the person who is operationally responsible for the process. So it is transparent and clear where responsibility for risk and safety of working rests. With what we are doing now I think that it is quite unclear where responsibility will lie, with which agency. Will we now be into a situation of dispute and argument between different Government agencies? That is something we have never had to contend with within the pharmaceutical industry; for products we have gone through the Medicines' Control Agency who ask all the right questions of us and demand a very high standard. For issues on worker and environmental protection and other aspects we have worked with the HSE. We have now introduced, through European directives, another overriding consideration; was genetic engineering involved? My reason for saying the American system is more transparent, easier to understand, and is much faster is because the notification periods are not in place. That then impacts upon cost because any delay in our industry has an effect on cost.

(*Mr Savidge*) These notifications and consent requirements are likely to be on the critical path for product development and therefore you could easily imagine a situation where there was a delay of up to six months because remember that under the stop-the-clock issues, if one is having to respond to questions and required to provide further information, then the clock is stopped during that period. A six-month delay on getting a product to market can have a profound financial impact because it knocks on right through the product life cycle affecting the time at which you achieve peak sales, all the way through the product life cycle that effect will be present, so the financial implication can be very significant.

Chairman

400. I am coming to the conclusion that you would like to see the European regulations scrapped and replaced by something rather like the present ones, am I right?

(*Dr Poste*) As a simple pragmatic answer, yes.

Chairman: Good.

Lord Renwick

401. Chairman, I see Lord Flowers is no longer here, but he did ask previous witnesses from Hoechst whether they had approached the deregulation taskforce. May I ask Dr Dewdney whether they have in the DTI? I know they are set up to look at regulations over a very wide range of industries and to help in situations like this.

(*Dr Dewdney*) We have had an input to the DTI work group on deregulation and this is coming in through both the company and SAGB.

Chairman

402. Are people listening to you?

(*Dr Dewdney*) I think it is early days for that.

(*Mr Savidge*) The other area where we have an input is through the trade associations, in our case through ABPI and through them into EFPIA, the European Federation of Pharmaceutical Industry Associations, into the Commission.

Baroness Platt of Writtle

403. Going back to the question of horizontal and vertical, from other witnesses surely one is always going to have an HSE input from the point of view of the effect on the people working in the industry, as far

[Baroness Platt of Writtle *contd.*]

as process is concerned. Surely you are always bound to have some horizontal?

(*Dr Dewdney*) Absolutely, yes. We have it now. That is in place and that is real.

404. I do think therefore—and I have said this before—that this argument between horizontal and vertical is a very misleading argument. You are accepting that it is going to happen in fact but it is the product you want to be safe but on the other hand clearly there are process elements that are equally important?

(*Dr Dewdney*) It is a misunderstanding of processes, I think. There has always been what we call "horizontal", in other words process legislation, handled by the HSE. It has worked extremely well with a tremendous record of United Kingdom safety for workers and the environment. To reinforce the answer, would we like to be more like the Americans?—yes we would. They have existing safety legislation and they do not see any reason to change it for GMOs. We could have done exactly the same, based on the extremely good record of the industry working with the HSE. That is horizontal process control.

(*Dr Poste*) If I could just add very briefly, the presentation of the American system as orientated towards product rather than process. There are clearly some processes that are hazardous in the context of worker safety and environmental safety. These apply to process rather than product but in the final reckoning there is a consistency about the integration of these requirements in the development of the product application. You do not have to file separate filings in relation to environmental and worker safety and other regulations. This can all be accommodated within a single dossier that is accepted by the so-called "lead agency". Given the fact it is a pharmaceutical product the Food and Drug Administration will take the lead. If the FDA has any concerns with respect to worker safety or environmental issues it will then consult with the relevant government agency but there is no formal requirement to submit to that other agency.

405. What you are really saying is that you are going to need both but it is the interaction of the European legislation which has brought a new factor into the horizontal side, are you?

(*Dr Dewdney*) It is the introduction of further agencies and horizontal control into product regulation; that is the issue for process it has always been there. No-one questions that. That is essential for our safe working and for the environment but it is the introduction of legislation for products. Our view would be that a drug or medicine must be shown to be safe and effective and to be regulated through the appropriate agency. It is irrelevant to the argument whether you use a GMO to produce that product. If you want further examples I am sure Mr Savidge can give you several from our own fermentation practices where we now use GMOs in our antibiotics production process. That is irrelevant to the safety of the final product which should be judged by a single agency. What European legislation has done is brought in three government agencies who all are going to want information on the safety of the product. So that is the difference.

(*Dr Poste*) We have touched on the semantics before if offered, I would like one opportunity to purge certain terms. I find the terms "vertical" and "horizontal" quite unhelpful.

Baroness Platt of Writtle] I do agree!

Chairman

406. I think you will find Lady Platt agrees with you very strongly on that!

(*Dr Poste*) If I can beg the Committee's indulgence, we would consider product, process, worker safety, environmental safety, product safety or all the other perceived hazards need to be approved horizontally or vertically.

Chairman] I have only known it or got used to "horizontal" and "vertical". I am not going to change!

Lord Walton of Detchant

407. As we have mentioned fermentation, can I ask for clarification? You say on page 9, "It is highly probable that most fermentation-based activities within the pharmaceutical industry will need to be within the classification Group B". I want to know why.

(*Mr Savidge*) I think most of them would be Group I, Type B. I would reiterate the point Dr Dewdney made that by definition such organisms are non-hazardous irrespective of the scale of operation. I wonder if I might just add one further point on this classification of organisms. We do believe strongly that a classification of a single group, i.e. Group I for non-hazardous organisms and anything which is not classified under group I therefore becomes group II is too blunt a classification. In Group II One is combining in one category a whole spectrum of risk from minor to major. I would have thought that it would be far better if Group II were sub-divided according to risk, and there was a graded response from the regulatory authorities in terms of notification requirements, and in terms of emergency plans so that they were concentrating their resources where they are most needed, in other words on the really hazardous operations and not spreading themselves too thinly into areas where there is very little hazard and the industry is quite capable of self-regulation. I am not saying that we should ignore those risks—of course not—but in terms of notification and the impact that the regulatory authorities are going to have on our activities they should really be concentrating their effort on the high risk category.

Chairman] We have come almost to the end of our time but Lord Gregson has a question and we will make it the last.

Lord Gregson

408. One thing that worries me about these fairly global answers say with regard to that fact that you would rather have the American regulations than the EC regulations, is you take them out of context, the context of the legal infrastructure etc that exists in American. The draconian effects of the environmental laws in America now (the EPA regulations and regulations on contaminated land)

[Lord Gregson *contd.*]

can wipe out a company overnight of course. Public liability problems in American are much more severe than they are in Europe for instance. There are constraints that exist in America that do not exist in Europe and they are quite draconian. They can wipe your company out over night if you step beyond that line. In effect you really are regulated by a much more absolute system than appears on first sight if you operate in America. Is that not true?

(*Dr Poste*) I think those are very legitimate caveats to be raised. The intent is not to argue that the US system is fully designed to address all issues. I think I would certainly make the case, as I know many of my colleagues in the industry do, that the US regulations have a far broader science-based content. It is not just simply a question of comparing the US relative to the European Community. The playing field is global. The key issue is that there are elements of the EC Directives themselves and/or any modifications that the United Kingdom may chose to apply to them which will place the United Kingdom and the EC at a disadvantage relative to Japan, the Pacific Rim and the United States? I would have to argue at the present time (even though I will certainly acknowledge many of the US problems with respect to the environmental issues and litigatious excess) that from the standpoint of pharmaceutical products and vaccines the US regulations would seem to be not only overtly science-based but are compatible with effective protection of the public and environment while allowing industry to work effectively.

409. I would suspect taking all this into account, public liability, contaminated land etc, you would not set up a plant in the US by choice at this point in time despite their easier regulations?

(*Dr Poste*) Far from it! One draconian element of the United States regulations in fact is that I am the named individual for 11 different regulatory agencies to go to gaol if the company does not comply. This is a somewhat sobering thought one has every morning.

Lord Gregson] The whole board goes to gaol—just to comfort you.

(*Dr Poste*) Undoubtedly, Sir, the regulatory climate in the United States will weigh very heavily on our decision to site a manufacturing plant in the United States. It would be unfair to say that that is the sole criterion. There is a significant issue for ease of technology transfer relating to existing units that are already there in the US. However, the US regulatory climate is viewed to be far more receptive and, again, returning to the science base issue, to the availability of the specific skills that we will need. While concern was voiced about the US, we felt that that the US had a marginal advantage over the United Kingdom.

Chairman

410. Thank you very much. You may wish when you have seen the transcript of the evidence to amplify some of the things you have said or give us any further information which you may feel would be of help to us and I sincerely hope you are not writing from gaol!

(*Dr Poste*) No. Thank you very much, Lord Chairman.

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HOUSE OF LORDS SESSION 1992-93

MINUTES OF EVIDENCE
TAKEN BEFORE

THE SELECT COMMITTEE ON SCIENCE AND TECHNOLOGY

(SUB-COMMITTEE II REGULATION OF THE UK BIOTECHNOLOGY INDUSTRY AND GLOBAL COMPETITIVENESS)

Thursday 29 April 1993

Sir Walter Bodmer
Ms J Hill

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THURSDAY 29 APRIL 1993

Present:

Flowers, L.	Soulsby of Swaffham Prior, L.
Hilton of Eggardon, B.	Wade of Chorlton, L.
Howie of Troon, L. (Chairman)	Whaddon, L.
Perry of Walton, L.	Kennet, L.
Renwick, L.	

Examination of witness

SIR WALTER BODMER, FRS, Director General, Imperial Cancer Research Fund, called in and examined.

Chairman

411. Good morning. I wonder, Sir Walter, if you would begin by telling us just a little about yourself for the record. You are well known to the Committee already, but perhaps you could tell us something of your background as it relates to this enquiry.

(*Sir Walter Bodmer*) My current position is as Director General of the Imperial Cancer Research Fund and until two years ago I was director of research there. I am a geneticist by trade and was previously a professor of genetics at Oxford and Stanford USA. My training is in molecular biology and genetics, but I started as a mathematician as an undergraduate. I have been, amongst other things, until recently President of the Human Genome Organisation and very much involved in the promotion internationally of human genome analysis. I can expand on that, but also of considerable concern, which I think is an element here, is the public understanding of science.

412. I get the impression that you know a good deal about the subject, if I can put it that way. We have had a good deal of discussion with witnesses about biotechnology and its relationship to new projects. We have had witnesses from industry and government and so on. Can you tell us anything about the relationship between biotechnology and basic science?

A. Yes, I am assuming here we are talking about biotechnology in a modern context.

413. Yes.

A. The manipulation of DNA and of cells. For the basic science I am involved in it is absolutely fundamental. In the sort of research laboratories that I have worked in and look after, virtually everyone uses some aspect of biotechnology work in what they are doing from the most basic to the most applied areas. If you are interested in the fundamental mechanisms of how cells divide, which has advanced enormously recently, biotechnology uses recombinant DNA techniques to find the genetic changes that lead to the identification of switches for turning cells on and off in cell division. You can study the expression of proteins, the regulation of expression, and you can study differentiation, so essentially all aspects of basic biology. Evolutionary studies, even going into the social sciences area, for example physical anthropology and the study of the relationship of different populations to each other, nowadays also depend on the application of biotechnology, knowledge, techniques, and the ability to study genes at the DNA level and so individual variations in a whole variety of new ways. It is just quite fundamental to all aspects of basic biomedical research.

414. You are closely interested in cancer and it is not too hard to guess that there is a strong link between cancer research and biotechnology. Can you tell us something about that?

A. Yes, I suppose the starting point is that as a geneticist I was appointed to look after the research of one of the country's major cancer research organisations, the Imperial Cancer Research Fund, and genetics lies at the heart of what cancer is because in terms of the cells that go from the normal to the cancerous state, cancer is a genetic disease at that level. It is a series of genetic changes which gradually, in a sort of soematic evolutionary process, take the cells from the normal to the abnormal. So the fundamental challenge in cancer research is to identify those individual genetic steps, and then to make use of that information in the prevention and treatment of cancer as a disease. Therefore, in our laboratories at the Imperial Cancer Research Fund out of a total perhaps annual expenditure of something over £50 million, I would say that somewhere between £20 million and £30 million of that is in one sense or another connected with work in biotechnology at all sorts of levels. I could give examples. There are remarkable advances in our understanding of those fundamental genetic steps, particularly as they relate to the control of the division of cells and the way that, in a cancer, that control is in a sense usurped by the cancerous cell so that it can grow independently of its immediate environment and be stimulated to divide itself. That discovery is dependent on finding the relationship between the so-called oncogenes, the genetic changes which were discovered through studies on viruses that cause cancer, and the growth factors that stimulate cells to divide. That is now leading to new approaches to the treatment of cancer by blocking the effects of those growth factors. In a totally different area, one which I am personally involved in, we study a lot of the rarer, but nevertheless important, inherited susceptibilities to cancer because we know that when we find genes that identify those susceptibilities, they may also be genes which are critical for the development of the cancerous process even when it has no relationship with the familial situation. For example, in bowel cancer where about half a per cent of it is due to a particular inherited abnormality, through work we

[Chairman *contd.*]

have been involved in and others, the gene has been found and shown to be crucial to the earlier stages of perhaps 70 or 80 per cent at least of all bowel cancer. I am just giving you examples here of work that depends on very sophisticated application of biotechnology knowledge and indeed depends on the whole area of the human genome project for mapping genes that influence disease susceptibilities. Even in that basic underpinning area of research, where we have been very active, we spend something of the order of £4 million a year on that. That is part of our overall expenditure on biotechnology, and is representative, I think, of any organisation in the biomedical research area nowadays.

415. I can see readily enough where what you might call genetic engineering could play a part in research of this kind, but you did mention treatment in passing. Is there much in the way of treatment deriving from the technology?

A. Well, I believe that the whole future approach to dealing with disease will depend on what we find out ultimately from the human genome project and what comes from the application of biotechnology to understanding the human genome. That applies in the cancer area as in other areas. I think there will be a variety of ways in which that happens. New products are found which are the direct products of genes which may be used in treatment. Interferon has been used, for example, in the treatment of cancer. Various growth factors have been used. Through the knowledge of those new products, new assays have been developed for new chemical entities for the treatment of disease. I mentioned earlier growth factors, but in many other areas where you have got receptors for various substances in the brain, for example, the way to analyse them nowadays is to find the genes, find the variety of factors, of different types of receptors and devise assays which are more selective for particular functions. All of that depends essentially on the use of biotechnology to discover new treatments. In the area of prevention, consider the one area I mentioned, of bowel cancer. Through the knowledge of that gene we now have a specific mouse model for that form of cancer which gives rise to pre-cancerous growth, and that animal model gives a very specific opportunity for studying factors which might prevent those growths. So the prevention area is important. Another example is the study of genes which, when they malfunction, decrease the ability to repair damage to DNA and so give rise to increased susceptibility to cancer. In other areas, variations in the enzymes which are involved in heart functions, have been shown to be important in susceptibility to heart disease. In general, in fact, cancer is the least heritable of human diseases. Most of the major human diseases we face now—mental disease, heart disease, the autoimmune destructive disease like rheumatoid arthritis or juvenile insulin-dependent diabetes—are genetic or have large genetic components, and the human genome project is the route to identifying inherited differences in susceptibility to those diseases. I believe the route to a more targeted approach to prevention will be by identifying individuals at risk and through that being able to apply prevention approaches, either drug or dietary recommendations or other approaches, more effectively. So I think the whole of the future of the way we deal with disease and health, the future of the pharmaceutical industry, is going to be totally dependent on the application of what is broadly called biotechnology. It is the most productive application; it is going to be a very productive industry which is important to encourage.

Chairman: That is a very positive statement.

Lord Renwick

416. Could I ask Sir Walter to follow on from that fascinating look into the future from what has happened over the past, and tell us if regulations have hindered up to now the research which you have been conducting and which has been conducted into cancer and heart disease?

A. I think minimally, but I would like to make a general statement about the question of regulations. I was involved in Lord Ashby's initial working party on recombinant DNA, as was my colleague, Sidney Brenner, who should have been here this morning, and in that debate—

Chairman

417. When was that?

A. That was in 1974 and 1975, when the debate about the potential risks of recombinant DNA work was raised. I have to say, and I believe it is not with hindsight, right from the start I felt there was no real issue of risk. The risks were raised, I think, by concerned individuals, scientists, who perhaps on the one hand did not fully appreciate working with microbes and understand the issues of micro-biology and the fact that pathogens, dangerous organisms, are dangerous to work with whether you manipulate them using recombinant DNA techniques or not, and if you manipulate them they become safer. Nor did they fully understand basic evolutionary principles. My background as a population geneticist and evolutionist would tell you that on the whole, if you change organisms in defined ways they are very unlikely to have an intrinsic evolutionary advantage. So I feel that even the regulations we have now, which we live with, which produce a lot of paper and require us to have more people to deal with providing the information than we would otherwise need, are to a fair extent unnecessary. But, of course, we work with them, we live with them, and the larger the organisation (and compared to academic institutions my organisation is large) the easier it is to handle them. So I think probably one can say there has not been in this country a major draw-back through regulations. There have perhaps been times when things have been held back somewhat, but I think mainly there is unnecessary expenditure of effort. In my own laboratory where I am involved, perhaps indirectly rather than wielding a pipette myself, in recombinant DNA work there are other issues which are far more important, even though those themselves are not that risky—handling materials from human individuals who may have infections is a far more serious problem in practice for us than working with microbes which have no pathological consequences in circumstances which are really quite safe. I would emphasise that as a general view, and

[Chairman *contd.*]

that the issues of regulation which occur are those which relate to pathogenic organisms.

Lord Renwick

418. Could I follow that up by asking whether regulations in other parts of Europe have restricted people of enormous calibre in those countries from contributing to this?

A. Yes, I believe there are some very serious issues, and these have arisen particularly in Germany and to some extent in Switzerland where I know less about it. I am afraid it is political attitudes, not in my view served by the science which must be the ultimate determinant of whether and what sort of regulation is needed, which have introduced considerable constraints and have made it difficult for colleagues of mine in ordinary working laboratories to cope with those regulations, and have been a serious disincentive to the industry. My concern for this country would be not to see worst practice spread throughout the European Community from other countries, and it is something we should be extremely cautious about.

Lord Soulsby of Swaffham Prior

419. Sir Walter, you painted a picture of massive expansion in the field of biotechnology based on the human genome and the spin-off there. Is the science base in this country sufficient at present to handle that?

A. You must expect me to say I would want the science base to be larger. Having said that though, what I would want to emphasise is that in the biomedical research area the contributions of the medical research charities, of which I am one and in which now the Wellcome Trust makes an enormous contribution, are absolutely critical to the level of high quality medical research in this country. They are substantially more than the contributions of the Medical Research Council and without them I think there would be a very serious situation. I think it is important to emphasise that, and that those contributions are not only to the basic research, they are to the training of people who go into industry and to the general reputation of this country in that area. I do not want that to be in any way interpreted as a negative comment about the Medical Research Council. They have supported and continue to support excellent work, but if you are talking about scale in the biomedical research area, without the contribution of the charity sector, this country would be in a very, very poor situation. I am sure there are areas in aspects of biology which might not be covered in the same way, and I am talking here about the more fundamental and what you might call broadly academic research, where that sort of support is not available, and of course some of the under-pinning areas in the physical science where in my view, in areas of chemistry and physics, there is clearly not adequate support. So I would not feel at the moment that things are totally inadequate. I think we have a very good biomedical research activity but I would not be complacent about it, and I would emphasise those contributions from the private sector.

420. You have mentioned the problems in Germany and to some extent Switzerland, and of course that is, I am sure you will agree, having precisely the depressing effect on the science base which you mention, not only in terms of research but training young people?

A. I believe that is the case. I believe it is a difficult situation in Germany in particular at a time when its basic research in biological areas should be flowering. I have not in this context said anything about the level of biotechnology research in industry—I am sure you will have heard a great deal about that from others. It is increasing enormously and it could go a lot further and we may have an opportunity to talk about the sort of start up industries which have been so common in the States but less common here.

Lord Flowers

421. Before Sir Walter does that, I wonder whether he could go back to what he has been talking about? Wearing your COPUS hat, if I may suggest it, what is it really about Germany, and to some extent Switzerland, which has led them down a different path from that which the rest of us are trying to follow? It sounds as though you consider what they have done is unreasonable and unhelpful. It must arise from political pressures, if you want to call them that, which reflect perhaps a misunderstanding of the nature of science, or something of that kind?

A. Might I just expand a little on COPUS, the Committee on the Public Understanding of Science, which at the moment I chair. It is jointly supported by the Royal Society, the British Association for the Advancement of Science and the Royal Institution, and supports many initiatives in this area. I do believe the public understanding of science, is absolutely critically important, particularly in areas like this so that the public has at least some understanding of the issues which do arise, so that they can appreciate the benefits that can come and is not afraid of terms like "genetic engineering", which can be very widely and inappropriately interpreted often to mean tampering with eggs and sperm and the future inheritance which is very far from anything that we do. I think the problem in Germany is partly in relation to its history and a concern about the applications of genetics. I think it is quite an inappropriate concern of their application in the human area and indeed I was intrigued the other day to have contact with a colleague who is the Vice President of the Max Plank Institute where they are planning a major new institute in human genetics, and wanting to set a lead in this area to show that is what science should be doing. I think myself that that history is being taken advantage of politically by some of the groups, those who are concerned about environmental issues but perhaps not in the rational way that one should be, and using this as an opportunity to attack, I think, in a quite irrational way. I think the public understanding of science is really quite crucial in that area and relatively small investments can have a major impact on the acceptance of new technologies in a variety of ways.

Lord Perry of Walton

422. I have a question which is that if relatively small contributions do not reach the majority of the general public, would it not be rather more expensive to achieve a general public change?

A. Yes, and I think my reference to "relatively small" is when I look at the budget of COPUS and what we have asked the Minister of Science to support. An extra £1 million or £2 million can go a long way in acting as a catalyst for a lot of different activities and of course those activities need to get to a wide public. They are activities beyond school education, of which you are all too familiar, of influencing the broadcasters, getting adequate presentation on television of scientific issues, but of course also not forgetting the tremendous importance of education in schools and how much one can do with proper school education in this area, which is where it must all start.

Lord Kennet: Chairman, may I put a question? I ask your permission because I am not a Member of the Committee?

Chairman: Certainly.

Lord Kennet

423. Do you ever think it would be wise to accept the present burden of regulation and keep an eye on the future when it having been proved over various generations, fairly short for some species and fairly long for others, that there is no harm in what is being done that the regulations may be modified and even withdrawn?

A. I am concerned about that approach. I think there is a tendency for the regulation to escalate and never to go down and I think that tendency really has to be fought. There is always the possibility of making a mistake, but I do not think there is any greater chance of doing that with the recombinant DNA technology than in any other areas that involve biological research, and I have to say that I think there was no real justification for the initial regulation in recombinant DNA work and I think subsequent experience has documented that. There are no examples, to my knowledge, of any adverse circumstances of recombinant DNA work as such. It is not very easy to do the epidemiology of that. It seems to me that to focus on these minimal risks might even divert interests from other areas of safety and environmental questions that are more important.

Lord Perry of Walton

424. Is that statement, which is very sweeping, equally true of the release of genetically-modified organisms or plants?

A. Well, that is a different area and one in which I am less expert, but I would make comments somewhat along similar lines. I would say that just in the same way that I think the evolutionary principles that led people to be worried about the release of genetically-modified microbes, I think inappropriately, which were not understood, I think the same applies, for example, to the modification of plants. It is not obvious to me why a plant modified by recombinant DNA to be resistant to an insect or to be able to withstand some chemicals should be any more dangerous than the attempt to do the same by interbreeding the plant. You have a more defined end product using the recombinant DNA approaches which should be easier to understand and better described, so it is not clear to me if you compare the two that there is any greater risk, and probably lesser risk, from the plant genetically modified by biotechnology than that genetically modified over the last 10,000 years since the beginning of agriculture.

Lord Flowers

425. Do you think the Royal Commission on Environmental Pollution ten years ago were wrong to point out that there were certain risks which had not yet been evaluated and perhaps should be?

A. I think I would hesitate to say that because I think there clearly could be certain situations where the risk is going to be greater if you release something that is biologically modified. But I am not sure that in general that risk is greater than the risk of bringing in or introducing species from Latin America to Kew or to having new approaches to hybridisation between, say, cultivated crops and their wild progenitors and trying to introduce new variations. So it is that comparison, where we have seen many examples of the inadvertent introduction of other species that should be considered. What I am saying is it is not clear to me that the recombinant DNA approach introduces major new principles in that. It might even make it easier to deal with.

426. You would not bring up the same strictures against the Royal Commission?

A. No, I think these are issues that need to be looked at and they may be broader than the application of the recombinant DNA technology for example to cancer. But, for instance, I think, a lot of the applications in the future of genetic experimentation will, as in the human situation, not necessarily mean the introduction of new genes, but the use of genetic markers to have a much more precise approach to selective breeding. Now it is not obvious that then when you have selectively bred something with a more precise use of genetic markers, that the result of that is any more or less dangerous than had you done it less precisely using more time and other more conventional approaches.

Chairman

427. You seem to me to be taking a sternly pro-scientific line?

A. Yes.

428. I thought I detected that! A little while ago you said something which has been put to us at least twice by industrial witnesses and that is that the genetically-manipulated item, whatever it happened to be, might very well be more safe than the natural one.

A. Yes.

429. Now, that may well be correct, but the public perception would of course tend to be in the other direction.

A. Yes.

430. In your role in relating science to the public, how would you go about persuading people that they were wrong when there was something which they felt was self-evident?

[Chairman *contd.*]

A. It is not an easy question to answer. I think that education about genetics is quite fundamental to education in biology and I think the more we do it starting from school onwards the easier it should be to explain to people that what we are doing is something that is not intrinsically dangerous. I spend quite a lot of my time, for example, talking to volunteers who raise money for the Imperial Cancer Research Fund as a charity and I very often talk about genetics, about the use of DNA technology, and I do not get a response when explaining what it is that we are doing that indicates any concern in those areas, so I think a great deal is dependent on proper explanation. I think also we know too little about the effects of the use of certain terms which are emotive and of which I would use "genetic engineering" as one. It may be that we should try and understand better, in the way that a good investigator for an advertising promotion does, what the impact of different terms on the public is and how perhaps to modify the use of words in ways which are more acceptable. Those are not terribly specific answers. I think it is a continuing process of education at all levels, and education really to impress on people that in the end it is for their own benefit, that they are going to benefit from knowledge of genetic differences in susceptibility to disease. When you say that I am bullish for science, I am, but that does not mean that I ignore the need to discuss the implications of what we are doing. I think there are implications in what is done with knowledge about genetic viability, but some of the concerns particularly related to safety have been, in my view, inappropriate.

Chairman] Somebody mentioned to us yesterday that biology at school was thought to be a girlish subject, that boys went in for more manly enterprises like physics and chemistry. Is there anything in that?

Lord Flowers

431. And the teaching of them were in conflict, so far as the timetable was concerned.

A. I am a strong proponent of teaching balanced science in school and of not having the narrowness that we have in our A-levels, not allowing people to focus only on science or only on arts and humanities at that level. I am also a proponent of a balanced education between the sexes, and since biology is at the forefront of science it seems to me to be no bad thing if more women are going into biology. Biology teaching is bound to be changing. It is becoming less of the birds and the bees and the fur and feathers brigade, and in that area itself you can have more complex science and contributions of mathematics to population biology and ecology than in many other areas. So I would not be unduly worried about that. I would also say if people are interested in the natural world around them then that is an entry to an interest in science, as witnessed by the large number of children who go to and enjoy the Natural History Museum. That must be a good thing and we should use that route to a more fundamental understanding of scientific issues.

432. Would you say there was an essential element or need for doing a bit of mathematics and biology, when one is talking about things like safety? I remember a parody which was run by O R Frisch of the nuclear safety problem where he pretended to propose for the first time that coal should be burnt in the domestic grate, and you had to do a safety analysis of this of course and there was the possibility that the coal might set fire to the chimney and so on, and gradually a horrendous, catastrophic situation developed where a whole town was destroyed, but the whole point was that no numbers had been put in; if he had put numbers in the case would have been destroyed immediately. Very often with these safety assessments, so-called, done by various people on the nuclear side but also for problems like the one we are supposed to be discussing today, no numbers are put in, and so all these wild dangers are put forward which have a probability of 10 -59 or something like that.

A. I would have to say that numeracy is extremely important. Not everybody can understand maths to a level that one might eventually want to achieve, but I think everybody should understand something about numbers and the meaning of numbers and statistics and probability in general. I think any scientific education must have a quantitative basis, and in my personal experience, starting off as a trained mathematician in Cambridge, that background has been extremely valuable. I think we have enormous problems in the public perception of risk which are relevant to this; the notion that there is such a thing as zero risk, any notion of relative risks of one sort or another. I think those are major issues and the public understanding of science will depend very much also on the public perception of appropriate risks and their assessment.

Chairman

433. I must say this touches on an uncomfortable person experience of my own. I wrote an article in a magazine I am connected with about acceptable risk—this by the way for an audience of engineers who should really be well acquainted with such an idea—and there was quite a large response and correspondence from people who said that no risk was acceptable—a wonderful idea but not very sensible. Going on from there, I am told that Dr Brenner has devised a risk assessment method and that it does put numbers on things and has been adopted by the Health and Safety Executive. Do you know about it?

A. Yes, I do. I produced a report for the Royal Society at one time criticising it.

434. You did? Criticise it now!

A. I think it has been a useful device. I think the difficulty is, can you put precise numbers to the parameters which you want to use. It is very difficult in many of those areas to do that. I think, nevertheless, it has turned out to be a very useful guide and it is used in practice and we have within my institution the required Recombinant DNA Committee which uses those assessments, and I think it satisfied a need and continues to do so. But I think inevitably one should not put too much emphasis on the particular accuracy of any given estimate of risk.

435. Some of these things are difficult to assess. You will remember Colin Buchanan's famous

[Chairman *contd.*]

remark of many years ago, "How can you put a value on Stukeley Church" when he was doing a cost benefit analysis.

A. Yes.

Lord Whaddon

436. Has any desirable research been squeezed out of the United Kingdom by any of the present regulations? Do you feel there is such a risk in future from the proposed new regulations by the Commission?

A. I suspect the answer is, to your first question, no. I think the concern I have is just a gradual escalation—and I have asked my colleagues in the safety area in my own institution what their view is and their concern is particularly at the increasing amount of paper and information which is required, which increases the cost of search support. We manage it, we pay for it, obviously, and that in a way means there is a little less available for other things. But you live with that. It is like in the area of animal experiments, the amount of information we have to provide and the control which is needed just continues to go up. While, of course, safety is extremely important, it must be based on the best science, and a rational analysis which looks at the cost benefits of what you are implementing, and I would suspect that the extra cost of what we have to do actually give us no particular benefit. So I would be concerned that this should be an area which is monitored very carefully to avoid that feeling, "It doesn't matter if we ask for a bit more to be produced and a bit more" and gradually escalating more and more controls in ways which are not really productive, and perhaps even not doing some of the investigations which one should do if you are generally concerned about them. There have been attempts, for example, to monitor the incidence of cancer and other diseases in workers in institutions such as ours—they are difficult to do and they have not yet been very successful but that is at least a positive attempt to see if there really is anything you can identify which is a significant risk.

Lord Wade of Chorlton

437. You mentioned earlier the political attitudes towards establishing regulations. Do you really believe these political attitudes could be now holding back benefits which society would otherwise have if the regulatory system was less politically motivated?

A. My main comment on the politics was with respect to Germany, and I would not want that to be applied to this country. We have not to my knowledge had that sort of bias here. If you look at things on a worldwide basis, there may always be some places where it is easier to do things than others, and the obvious strategy for the German industry is to move their production and research in areas which they feel are being constrained across the border into France or somewhere else. So what one would face if things escalated differentially between countries is the potential of a serious disadvantage to research and to economic progress dependent on that. I do not think we face that yet in this country and I hope we never do. I think this is an area of research that is enormously productive and we should encourage that and we should encourage innovation and encourage the development of new industries and new companies which are the seed corn for the variability of work, an evolution by natural selection which leads to the new successful companies of the future.

Chairman

438. So you are not very keen on regulations, but you are obviously quite keen on the expansion of industry in this area we are talking about. Now, I can see that the regulations might be a nuisance and of not much help to you in the lab conditions of containment and so on where everything is fairly tight.

A. Yes.

439. Now, would you hesitate a little on the industrial scale that containment problems must be greater there and regulations must be more necessary?

A. Well, I think it is clear that as you scale up there must be more problems and I would not claim to be an expert in that and I think it is clear that those problems need to be looked at in a variety of ways. They may even be problems to the individual of a greater risk of allergy to things which might be released when you are dealing on a much larger scale. So I think there is a need for some regulatory authority to be there to explore these issues and I think what I am arguing for, and strongly because perhaps the tendency is often in the other direction, is that that regulation is looked at in a careful, scientific and rational way and one always tries to make sure that the costs and benefits of that regulation are properly balanced.

Lord Renwick

440. Can I follow on from that, my Lord Chairman? It seems that Sir Walter has postulated that the regulations are an evolutionary system and that they can be altered. It has been hinted to us that the regulations in the United States which the industrialists seem to prefer at the research end can be adversarial. Can you comment on that?

A. No, I am afraid I do not think I know enough about that to comment. No, I am not aware of this problem. There are differences, but in the general research laboratory environment I would not be aware of major differences in the ease with which one can do research in the sort of laboratory that I work in, between the United States and here. I think it is very important to keep things on a par with the United States because the scale of the work there, whether it is in this area of the regulations or the FDA and its equivalent, is such that if we do not keep in line with that, we will be potentially seriously disadvantaged. But I do not see any major differences, at least at the level of the research laboratory, that I am aware of.

441. To go back to the first part of my question, you are confident that the regulatory system is evolutionary?

A. It seems to be, although it seems to be largely in one direction.

Lord Perry of Walton

442. We have been told by industry that they share your view to a very large extent that there is no great hold-up in terms of their research and the regulatory system is not being a penalty to this country at the moment. But we have also been told by industry, and very clearly, that there is already very considerable penalty when you get the scaled-up situation and the regulations there are very much part of the problem and that already in their opinion the likelihood is that we will lose out on some of the manufacturing plants because of that.

A. I think that would be of considerable concern, although I am aware that some of the early scale-up, for instance, in the production of monoclonal antibodies was done by companies in this country, so I really would not feel I know enough about the particular issues there to judge them. But all I would say is that if that is true, then it is something that ought to be looked at very carefully because if there are inappropriate regulations on scale-up then we have the risk of not having the industrial production of products of biotechnology to the same extent in this country as we would like.

Lord Whaddon

443. I seem to remember that there have been a number of occasions when our own attitude to research has resulted in commercial losses to the United Kingdom. Have you any feelings on this? Should we exert more secrecy and what about patents?

A. There are a number of comments in that area that I would be pleased to make. I think they start from the view that we are only beginning to get the right sort of inter-relationship in the areas I am involved in, between academic research and industry. When I was a professor of genetics in Oxford in the early 1970s it was almost impossible to find anyone you could go to who would know anything about how to contact industry if you had some interest in that, someone who would understand the issues. I think one of the first and most important things is to continue to improve that climate. I know I have learned from my present job what one can do and needs to do in promoting the interaction between academic research and industry I believe one can do that without holding back academic research, that you can in fact get quick and early patent protection if you want it during the time that a paper is about to be published. If you organise things properly, as we do, so that every paper is looked at for its potential patentability and for its market potential but in no way holding back its publication, you can manage that. I also find that many of my colleagues, sometimes quite distinguished colleagues, simply do not understand, (and I would not claim to be an expert), the whole range of issues around intellectual property rights. They do not understand that a patent reveals something and does not hide it, they do not understand that when you have got a patent it does not stop you from doing research in the laboratory, and I think they do not understand some of the needs for commercialisation. I would argue that a part of the educational process, and we were earlier talking about the public understanding of science, includes their need for educationin these areas. We should aim to get a much better appreciation, starting with young scientists going into research, of the issues of how to work with industry and what is needed. You cannot move forward without at some time having appropriate protection of intellectual property rights, and this can, and should be done, in an academic setting without inhibiting the free exchange that is characteristic of the enterprises of sciences. I have been very involved recently in discussions of the whole range of issues concerning the patenting of DNA sequences, where this question has been much discussed because of, in the view of many including myself, inappropriate attempts at protecting certain types of information on DNA sequences at too early a stage before the requirements of at least utility and non-obviousness have been satisfied. I have been involved in what I believe are very productive discussions with leaders of the patent law in Europe in trying to come to some consensus between scientists and the patent lawyers on how one can deal with that and get in that area the best balance between a free exchange and collaboration in the promotion of the human genome project, and the appropriate protection of novelty and utility which comes from the use of products which will be derived from the human genome project.

Chairman

444. We are running out of time, so I would ask one last question. A witness from the Department of the Environment told us that he took "the very strong view that differentiation between horizontal and vertical [regulation] is academic if the regulations are risk based..." Some other witnesses disagreed with that. Do you have a stance on it?

A. Yes, well, I first educated myself as to the difference between vertical and horizontal!

445. And took a long time!

A. And took advice from my colleagues, and I think there is an important issue there which, as I understand it, is to distinguish the control of the product itself, its purity, (and we are talking now about FDA type medicine commission regulations), from the process which produces that product. The view is that when it was chemicals with simple structures, or even complex ones, but nevertheless produced by a well defined approach, you would look at the chemical and you would look at its purity and that was a straightforward business. Many of the biological products in the past arose by from rather complex processes and were not easily defined as end-products. Therefore the process by which they were produced was regulated rather more than the end-product itself. I think that that situation has changed in that the products of biotechnology—a protein which is produced using a recombinant DNA technique or a piece of DNA even if it is inserted into some vector—can be very clearly defined as end-products. Therefore it seems to me that one should argue it is the end-product which should be controlled more than the process, given that we have the technology to do that, and that to try and institute both is certainly inappropriate. More thought ought to be given to what tests are appropriate to control the purity of products which come out of biotechnology, and to make sure that we

[Chairman *contd.*]

remain appropriately in line there with overall European regulations and with the Food and Drug Administration in the States, because no one is going to produce something in this country without having an eye to satisfying US FDA regulations. So I think that is an important area. I think my answer would be I do not believe it is an equivalent and that more emphasis ought to be put on characterising the product in the biotechnology area.

Chairman: Thank you very much. We will have to draw to a close there. You will have a chance to see the transcript of your comments, and if you wish to illuminate your comments further we will be very happy to hear from you.

Memorandum by the Green Alliance is printed separately

Examination of witness

MS JULIE HILL, Director, Green Alliance, called in and examined.

Chairman

446. Good morning, Ms Hill. Thank you very much for coming. Thank you for sending in a paper which we have all had a chance to look at. We did feel that an investigation of this sort would hardly be complete unless there was a comment from such a person as yourself. For the record, would you tell us what the Green Alliance is and what your fundamental attitude is towards this enquiry?

(*Ms Hill*) Thank you. I am Julie Hill, Director of Green Alliance, which is an independent, non-profit environmental lobbying group. We have had an interest in this area since roughly 1987 when we became aware of campaigning in the US on biotechnology issues and in particular to the deliberate release to the environment. We hosted a visit to this country of the US biotechnology campaigner, Jeremy Rifkin, and introduced him to a number of the regulatory agencies, to the press and to other environmental groups, and we kept a watching brief on the issue from that time on. We also contributed to representations on the Environmental Protection Act, on Part VI of the Act, which was bringing into United Kingdom law the EC Directives, and we lobbied quite forcefully particularly on the access to information requirements within that legislation. Subsequent to that I was asked to join the Advisory Committee on Release to the Environment as a non-scientific but environmentally interested member.

447. I am still a little hazy about the word "alliance". Are you a single body or a group of bodies?

A. The word "alliance" actually refers to the original membership of the Green Alliance, which is some 350 to 400 people eminent in their field and also known for their concerns on environmental issues. A smaller group of people, which has increased since, was brought together in 1978 to lend weight to the basic cause of the Green Alliance, which was to get the environment on the political and public agendas. So the Green Alliance always has been a group aimed at persuading political institutions, and more recently industrial institutions, they must take on board the environment in the broad sense, and adapt their institutions to take account of environmental considerations. We do work very much at that level, of regulatory regimes and other institutional factors and organisations, rather than on particular issues. This issue is rather unusual for us in that it is one of the few issues on which we keep a very detailed watching brief on.

Lord Renwick

448. What is the relationship with Greenpeace and Friends of the Earth?

A. It is purely informal. We have a large *locus* communicating with and corresponding with and informing other environmental groups. We are not a formal alliance of those groups. The Alliance is one of individuals which basically functions as an extended patronage.

Chairman

449. So a single body rather than a group of bodies?

A. Yes.

450. Can you tell us how many members you have now?

A. Around 360.

451. So much the same as it was?

A. No, originally it was somewhere under 100. It has grown very slowly over 15 years or so.

452. That helps us quite a bit. From reading your paper I get the impression that you are not opposed in principle to the notion of biotechnology and genetic engineering—that is a horrible phrase, I must say.

A. That is correct.

453. Do you believe that there are clear benefits which can be derived from this technology?

A. I think there are potential benefits, yes, theoretical benefits.

454. They have not been achieved yet?

A. Very few products have been brought to the market, so it is very hard to assess the benefits.

455. You talk quite a bit about regulating these processes and so on, relating generally to the environment as a whole, which is clearly your major concern. At one point in your paper, paragraph 11, you say: industry "... must be able to demonstrate the environmental and other benefits of the technology, not just put them forward as possibilities", I suppose you mean theoretical there. How do you think that

[Chairman *contd.*]

can be demonstrated, unless experimentation and production and so on go on?

A. I am not opposed to experimentation or production so I do not think the question arises in that sense.

456. It has arisen, I have just raised it!

A. I am sorry. I am sure you are right that it would be difficult to demonstrate benefits unless there was experimentation and production, but I am not opposed to those things, so I hope that in time the benefits will be demonstrated.

457. So you do not disapprove of the research going ahead?

A. Not at all.

Lord Flowers

458. If you say that industry must be able to demonstrate something, fair enough, but in order that what?

A. All I really meant by that is that I find myself frequently in conversations with representatives of the industry and there comes a certain point where somebody says, "Unless we are allowed to go forward with this technology, we will not be able to feed the world" or "will not be able to clean up irredeemable waste." That is fine if those research efforts are directed at, for instance, crops which have relevance in areas where there is a clear food need, or directed to particular developments which are going to help, not if all they really mean is that they are developing a technology for western country use which they hope somebody else will pick up and apply and pay for in other contexts. That is what I mean by substantiating the claim. It is not good enough to say, "We will feed the world with this technology", when there is nothing which clearly links the particular company or industry or technology with a positive outcome.

459. I understand perfectly what you are getting at, but I will press you a little: if you say they must do something, you have to say they must do something before they do something else, otherwise it does not make much sense. So before they do what?

A. Well, my remarks were related to public acceptance. I think a lot of the industry commentary on this is saying, "We are trying to do something which we feel is of broad public benefit." If it was said, "We are trying to do something which will make somebody money", that is not hard to substantiate, but if they are coming forward with arguments, "This technology is to be our saviour" in some broad sense, there must be some detailed cases and arguments which back that up. That is all I meant. A lot of companies do see public acceptance as slightly conditional on putting forward those kind of arguments.

Chairman

460. In paragraph 3 you talk about the benefits being hypothetical, I suppose, and you say that it is difficult to judge their real usefulness. Then you go on to say, "The theoretical opportunities are meaningless without the willingness to devote resources to developing them into products." That really means that you accept what is happening at the minute, that is, that products are developed and resources are put into the development by the companies concerned.

A. Yes.

461. You did not mean public resources or anything of that sort, did you?

A. No, I meant, as I say, that if there are to be claims that certain developments will be environmentally or socially beneficial, one would hope to see appropriate resources being put behind those. If I can give you one example, the theoretical possibility of a malaria vaccine through this technology has been around for a great number of years, but nobody was prepared to pay for it because the markets where it would be sold are not ones which are noted as being particularly rich.

462. So you would be talking there about public money?

A. That is possible. I was not necessarily directing that remark to it. I simply mean that, as I say, if the public is to be persuaded that this technology has certain benefits beyond pure commercial or marginal benefits, then one must see those kinds of developments going forward.

Baroness Hilton of Eggardon

463. As I understand what you are saying, you are saying that in a sense they are making much too wild and large claims as a matter of propaganda.

A. I think in some cases, yes.

464. You would prefer to see them making smaller predictions on specific claims and concentrate on bits of research which they may know may be productive rather than an objection to the research in general?

A. Yes.

465. It is the wildness of the claims you are objecting to as propaganda?

A. Indeed.

Lord Soulsby of Swaffham Prior

466. Could I just take you up on what I take to be your criticism of people who say biotechnology will help cure the problems of the world in disease control and the rest? You rather implied that none of this is being done and I would put to you that in fact a lot is being done in the animal health field, for example, where biotechnology and genetic modification is helping to control enormously important diseases of animals in the world on which one depends for food and transport. You mentioned the malaria vaccine, but it is not true that no one is willing to pay for it; the World Health Organisation has put a lot of money into it. I think one has got to be cautious with these rather wide statements that it is easy to say the world food situation will be cured but no one is doing anything about it because a lot of people are doing a lot about it. I am afraid, well, I am not afraid, but I am afraid I am criticising you for not appreciating it.

A. Well, I have talked to a large number of United Kingdom companies and, as I say, the match between some of those kinds of claims and the particular lines of research in this country is not total and I am not at all denying that that kind of research

[Lord Soulsby of Swaffham Prior *contd.*]

and development is going on worldwide. I am simply saying there are instances where those kinds of claims are made in a very broad sense without that particular company necessarily being engaged in research that is directed towards specific ends.

Chairman

467. I cannot help feeling, Ms Hill, that you are riding two horses at once here, but as James Maxton once said, if you cannot do that, you should not be in the circus! Can we move on a little bit to talk about food? Would you say that foods which have been developed through the use of GMOs were different fundamentally from natural food?

A. It entirely depends what they are. Some might be and some might not be. It depends what the end product is. The genetically-altered tomato, for instance, which has its genes rearranged—well it really depends what you want to construe as fundamentally different. Clearly in almost all respects, except at the level of its genetic code it is identical to the original. On the other hand, one can envisage the theoretical possibility of creating an entirely new food with this technology, so it may or may not be.

468. Supposing we stick to the tomato, do you think the genetically-modified tomato is a different kind of food from the one we know so well?

A. Well, at the level of its genetic code, yes, it is. In most other respects, no, it is not.

469. But insofar as it is a food, is it different?

A. It will presumably have been through all the appropriate procedures to ensure that it poses no greater risk to health and safety than a natural tomato, so in terms of its nutrient quality or the degree of risk it poses, I think probably not. It really hinges on what you find important in the idea of fundamentally similar or different. I am not quite clear what—

Lord Wade of Chorlton

470. What do you find important? That is what we want to find out.

A. My concern is for the environmental protection and, therefore, the potential ecological risk of any genetic development whether or not it is a food, and it is not really with food *per se*.

Chairman

471. Do you think that genetically-produced food ought to be labelled?

A. I acknowledge that this is an extremely difficult issue. My interest in labelling is that there is a large constituency of people, both consumers and those interested in the possible environmental effects of these processes, who are interested in knowing by what kind of process food has been produced, and I think that constituency is large enough to warrant efforts to examine whether appropriate labelling could be derived. I would not like to suggest that I have any very clear answers about how that labelling should be done nor deny that it is extremely difficult when you have got extremely complex food production processes and the point at which a modification has been made may be a long way back down the chain to come up with anything which is meaningful, however, I say, from the environmental perspective I would simply recommend that there is some effort to consult consumer bodies and other appropriate bodies as to how a labelling system might be evolved.

472. Let us get on to the ecology. What kind of ecological dangers do you see in these techniques, if any?

A. Again I think the risks are all hypothetical ones. Personally I have found the account laid out by the Royal Commission on Environmental Pollution in their thirteenth report to be the most comprehensive account of potential hazard, and I do not think that anything we have learned since has really updated our knowledge about how likely those hazards are to be realised in any given situation. That is the basic problem of risk assessment. We both have trouble identifying the specific hazards as an outcome of the release and attaching some measure of probability to the realisation of that hazard. Both those things are enormously difficult mainly because we know so very little about the natural environment and the way in which it functions.

473. Yes, I can see that. At the same time these hypothetical risks do not seem to have materialised, although it is only three or four years since the Royal Commission reported, so that is not terribly important, and it is obviously sensible to look ahead to try to identify hypothetical risks if you think they are there. At sometime, it is extremely important to try to assess the risk in some way and that would have to be some sort of mathematical way.

A. Well, at present it is not really mathematical. As I say, it is almost impossible to attach a measure of probability to any of these potential hazards. It is simply a judgment on the best available knowledge whether there is a broad likelihood or not of a particular type of problem.

474. It would always be on the basis of the available knowledge, whatever stage you were at, but at the minute the assessment of risk would be pretty subjective, would it not, and would be fairly crude in the sense that it would deal with things like higher risk or lower risk and that does not help us a lot?

A. It is the best we can do, I think, at present.

Lord Wade of Chorlton

475. Could I just follow on from that because we have had a lot of witnesses who, from their knowledge, their background, and university life, their academic skills and their very great involvement in this technology, have been very clear in their minds that this does not carry anything like the downside risks that your paper suggests it might. Why do you feel that your concerns outweigh their confidences? What do you know, or what do you feel you know, that makes you someone we have to take seriously?

A. It is rather the opposite. I think it is what we do not know. Speaking from my experience in ACRE, there is a body of scientific opinion which is prepared to acknowledge the large number of things we do not know about the functioning of the natural environment and the potential long-term effects of

[Lord Wade of Chorlton *contd.*]

releasing genetically modified organisms into that environment. I originally based my concerns on the extremely long and thorough enquiry by the Royal Commission, and I think their report is taken to have, I hope, a certain amount of credibility in laying out potential hazards, and I do not feel we have knowledge, in the three or four years since that was published, which tells us we can discount any of those potential risks.

476. In this particular type of technology, some people believe they know a lot more than you, and the ones who know are the ones who are most confident. But there are lots of other things which are developing in society which we do not know the result of either. We did not know what was going to happen when the motor car was first used. At what stage would you say we should stop this particular innovation because we do not know what its long-term impact is, and who makes that decision?

A. I am not saying we should stop it. I am arguing for a thorough risk assessment procedure, which I believe at the moment is being undertaken very well by the regulatory system. I think the particular character of this technology means we have to attempt to regulate it very carefully and that we are probably concerned about very long-term effects. For instance, one of the central uncertainties is what makes a weed a weed. What turns a plant which in some circumstances behaves normally, which is co-existing either in an agricultural environment or a natural environment with others, into suddenly something which is extremely competitive and potentially problematical, is not at all understood. If that kind of process is taking place it has been said that it can take 40 to 50 years before it becomes apparent or noticeable, so we are dealing with things on a long-term timescale which we have to make some effort to look at early and monitor. That is one of my central concerns, that we have some way of monitoring this and looking back at the kind of assumptions which were made. We are also dealing with something potentially irreversible. Almost every technology we have faced up to now, whether the development of the motorcar, chemical technology, even nuclear power, we can chose to stop doing. Nuclear power has certain irreversible aspects as well but we can chose to stop using the technology. If there turns out to be a problem with an organism released into the environment, particularly at microbial level—and I must stress some of my worries are not so much with the crop plants which are commonly being transformed at the moment but with the use of microbial and viral agents—if there was a problem as a result of a modification in the ecological sense it is (a) likely we will not notice it for some time and (b) when we do notice it, it could be extremely difficult to remedy. Those two particular factors make this technology much more worthy of our attention and a precautionary approach than almost anything else we have ever done.

Lord Soulsby of Swaffham Prior

477. The concern that you express of course assumed a high profile in the United States ten or fifteen years ago when the regulations were very strict indeed. But over the years the evidence from a very large number of sources has come to suggest that in fact the fears expressed ten years ago, shall we say, by individuals who held these views probably rationally at the time—and you have heard Sir Walter Bodmer comment on this prior to your evidence—are increasingly non-justifiable. My question is: would you wish to uphold your position of believing they are justifiable in the face of the increasing evidence that they are not justifiable, and what is going to make you change your point of view?

A. Can I clarify what you feel my position on this particular thing is, because I am not sure I have put forward a position which is total to the whole technology, other than saying that I am in favour of risk assessment?

478. I understand.

A. My position is that I am in favour of extremely careful risk assessment. I am not sure I can be presented with any evidence on a particular development or crop, or whatever it is, which will make me say that I am not in favour of careful risk assessment. It may be evidence which makes me feel confident that the requirement for risk assessment in the future may be less stringent, or the amount of consideration given to those developments could be less stringent, but I do not envisage reaching a point where we would say we would not want to scrutinise developments brought forward under this technology, because they will be constantly changing.

479. I would suggest that your demands in paragraph 4 are such that it is almost impossible to make progress. If you are going to demand such assessments, no product from biotechnology can be put into the market place.

A. I disagree with that. If that was the case, I would have been sitting on the Advisory Committee on Release to the Environment opposing almost everything that went through, which I have not done. I have been satisfied by the judgments which have been made and the releases which have been made in this country, because I feel enough attention has been given to the issues and enough caution expressed for the monitoring procedures to do the best we can, and I stress that. I do still think there are genuine unknowables in the long-term effect of release, but we must do the best we can at the moment in judging possible environmental effects. I disagree with the implication that urging precaution and risk assessment means nothing can go forward. If I can make a point about experience: my view, which I accept is fundamentally different from some of those who are actually handling these things, is that it is not enough to say, "Ten or fifteen years' experience gives us confidence in a broad sense in the technology". It may be there is confidence in making the judgments, in the sense that the arguments have been rehearsed and the evidence has been brought forward and there is a certain confidence that judgments about particular crops or particular transformations are broadly in the right direction and therefore those proceed rather more quickly than we have been able to do before. I do not think that amount of experience necessarily gives us confidence in the long-term about the overall effects of the technology. All this suggests that we should still scrutinise any new

[Lord Soulsby of Swaffham Prior *contd.*]

proposals and developments coming forward. So I do not think one can apply experience in particular areas to the implications for a regulatory regime overall.

Baroness Hilton of Eggardon

480. You are saying you are reasonably content with the present regulatory regime?
A. Yes.

481. But would not want to see it relaxed until we have further experience?
A. There are different ways of approaching relaxation. I would not want to see an abandonment of a horizontal system which seeks to look at applications of this technology.

Lord Perry of Walton

482. The evidence we have obtained from the manufacturers would make me believe there is not anybody who disagrees with the need for risk assessment. I would have thought that now goes without saying. The problem is in determining whether you can in fact in any sense put down risks to some of the things you have mentioned in paragraph 4. Do you really believe that anybody can make such an assessment?
A. I think there are genuine unknowables and I think there should be more effort to investigate and acknowledge what those are, and understand whether they do imply that certain lines of development should not go forward.

483. Do you think there is any conceivable way of doing such an investigation without releasing?
A. Yes, I think there is. If one is considering viral agents, it is clear there are certain aspects of the functioning of viruses which we do not properly understand, and to put new combinations of viruses or virus particles into the environment does pose quite substantial hypothetical risks, and our lack of knowledge makes it very difficult to attach any measure of probability.

Chairman

484. Can I interrupt you rudely just for a moment? It is quite true, as you say, that it poses risks, but it is by no means evident that these risks are as substantial as you have just said. They might be substantial, but they might not be. As you said, they are unknowable.
A. Indeed, and if they are unknowable, we could be taking a risk that is anything from negligible to extremely substantial and society must make some judgment as to whether it wants to run that risk or not.

485. I want to ask you a question which is unfair, and I hope you manage to answer it fairly! You know how there is a theory of acceptable risk and some risks are thought to be acceptable and some are not. The Health & Safety Executive have what you might call a "league table" of danger in which the danger from nuclear energy comes out to be the least dangerous of all, as it happens. I am wondering whereabouts would you put the hypothetical danger from these technologies? Is it as little dangerous as nuclear power or as dangerous as crossing Whitehall on foot?
A. I think, to be honest, my Lord Chairman, that is impossible and it also the technology not homogenous. The difficulty I have had in discussion of this entire area is that a large number of people seem to want to treat the issues around this technology as homogenous; as if every application or development has an equal degree of risks or benefits or whatever else. It is simply not the case. There will be some things which are potentially much more risky than others, some kinds of developments, some applications, and they will have a similar continuum of benefits. I think one of the problems in this debate has been an expectation that regulators or politicians or the public must come to some one view about the taking forward of the industry. I think that is unfortunate and confusing and unhelpful.

486. I did say the question was unfair and it is a reasonable reply.
A. It is a perfectly fair question, but it is just very difficult to answer.

Lord Perry of Walton

487. Do you differentiate in your mind between the release of products from genetically-modified organisms which have no potential for replication from those products which do?
A. There clearly is in terms of risk assessment, yes. Clearly if there really is no potential for replication then the potential risks are likely to be much less.

488. Would you agree then that with the ones with no potential for replication there is less need for regulatory control?
A. The problem is that in order to come to a view that there is no potential for replication, unless one can delineate what conditions replication very finely in advance, one needs to trigger the regulatory system in order to come to that judgment. This brings us to the difference between vertical and horizontal regulation. I think there is a view that the existence of a horizontal system implies that every single development using that process means the process itself is inherently dangerous; which is not the case. The point of having a horizontal system is to act as a trigger, or a net, for kinds of development that one might have a concern about, so that the system can scrutinise those and decide whether there are grounds for concern and, therefore, whether or not some conditions should be attached to their use. As the system evolves, I think it is very likely that certain categories of application or development will be deemed to be able to be put outside the system. To some extent the level of scrutiny which there is already existing within ACRE means that certain applications do not need full committee discussion because they are the same kind of things they have seen before. If there is quite a clear view about what the implications of the transformation are, there does not need to be the same level of regulatory attention as there might be to something new, so those kinds of discriminations will happen. However, a horizontal system which acts as a trigger to those kinds of judgments, I would argue, will always be necessary.

[Lord Perry of Walton *contd.*]

489. What comes to ACRE is the release of the genetically-modified organisms, not the release or use of the product of a genetically-modified organism which has no potential for replication. It seems to me that there is another committee which deals with these other things, but "horizontal regulations" is a very broad term and at the moment it is taken to apply to anything which at any stage in its manufacture has any connection with a genetically-modified organism.

A. Not necessarily any stage. What comes before the Advisory Committee on the Release to the Environment is something which has been genetically modified.

490. And still is capable of replication?

A. Well, that depends on the nature of the experiment.

Baroness Hilton of Eggardon

491. Can I use an example and ask would insulin produced by E.coli come before it or not?

A. No.

492. The product is not genetically modified, although it has been used?

A. No, it is a contained use.

493. So insulin would not be one?

A. No.

Chairman

494. You quite rightly draw attention to the fact that there is a great variety of products of this sort and the element of risk would vary from one to the other, and we would agree with you about that. Do you think that these regulations and procedures should be streamlined to differentiate between these and perhaps this would require the investment of resources to find out what was actually really dangerous and what was not?

A. There is already some move towards streamlining in the sense of how much regulatory oversight is applied to each application, but mainly based on the fact that similar judgments or similar cases have come up before and, therefore, there is no need to re-rehearse the arguments. Now, streamlining could be taken further to mean a number of different things. It could mean less requirements for information to be submitted and it could, at the extreme, mean certain categories of developments or proposals being taken outside the notification system altogether. Personally I am not in favour of making those second two steps yet. I am not saying that it would be impossible or unacceptable in the future. Almost certainly the system will streamline, particularly on the basis of experience of making the judgments, but not necessarily on experience that tells us that those things are any more or less risky in the long term in the natural environment.

495. You have mentioned the word "environment" and it takes me to my next question. Right at the end of your paragraph 4 you call for the "long-term monitoring of the results of releases" and then you go on to call for an "increased provision of funds for research into the functioning of the environment into which releases are made". Is that not a fairly tall order if you consider that the impact on the environment, if I am talking about the same thing as you, is affected by all kinds of things which are quite different from these releases?

A. Well, that is the case, but I would argue that we should be making more efforts to understand the natural environment, not just because we would like to be confident about releasing genetically-modified organisms into it, but because we have now a political and a social objective to protect biological diversity and our lack of knowledge about the nature of that diversity and its functioning is a very real barrier to doing that effectively. I think we also need to know more about the natural environment to know the implications for future economic use of the environment, how the gene pool functions, and what effects and what kind of factors are important. We still often do not understand the basis of natural infections or diseases of crops, all of which is relevant to a broader understanding of the way genes move around in the environment, and the ecological influences of one organism on another.

496. You would not really be piling all of that on to this particular industry, would you?

A. No, I did not mean to suggest that it should necessarily be the industry that funds this kind of research. I think it should be global, and certainly there should be a United Kingdom effort, although there is nothing to stop interested companies funding this kind of research.

497. The environment is fairly big, so you will have to have an international organisation to do that. How important do you think it is that our regulations should be of such a kind that they do not unduly hinder the biotechnology industry or industries?

A. My primary concern is with environmental protection, in which case I will support a regulatory regime which I feel does its best to ensure that. Once that is ensured, of course, I would like almost anybody else not want to see any industry unnecessarily hampered, but I do not agree with the suggestion that there might be some kind of trade-off between our industry's competitiveness and the degree of environmental scrutiny implied. I do not think that is in any one's long-term interests.

498. You have a slight problem there, have you not? The problem is until such time we have found out how the environment works, you cannot really do what you are asking them to do, can you?

A. We can have a regulatory assessment system which does its best to understand the risks.

499. Quite.

A. There are those who take the position, I think with some validity, that because we do not know very much about the environment this work should be stopped. That is not a position which the Green Alliance has ever taken because, to go back to the original discussion, we do recognise the potential benefits, and clearly there is always an implicit trade-off of benefits to the risks being run in almost any area of society. However, I do not think it should be explicit to the extent of saying the industry is being in some way hampered by these regulations and therefore will not realise what to me are as yet

[Chairman *contd.*]

unspecified benefits and therefore we should relax the regulatory regime. That is not the kind of explicit approach which will help the industry in the long-term; to be seen to be opposing what I feel is a regulatory regime put in place in good faith, or not to co-operate with its broad objective, which is to try our best to understand what the risks are and apply monitoring to them to try to verify those assessments.

500. Are you not taking up a position where you are sceptical about unspecified and unmeasurable benefits but you are not quite so sceptical about hypothetical and unmeasurable dangers?

A. I would like to think I retain an open mind about both. I do not think I can make specific claims about the risks or the degree of risks, whereas I do on occasion come across rather specific claims about benefits. I do not want to labour that point; those comments were really to give a reminder to companies that they cannot argue for public acceptance without substantiating and bringing forward things which under-pin their arguments. It does not to me centrally bear on the risk issue.

Lord Wade of Chorlton

501. Clearly from what you say you appreciate that very good benefits can come from the use of biotechnology?

A. In theory.

502. You admit that?

A. Yes.

503. And you have said that has already happened and you must accept already very good benefits, certainly in the health field, have already derived from biotechnology?

A. Yes.

504. So you must agree that it would be wrong that any regulations or any system or any pressures should be now exerted on those potential good benefits coming through which could quickly benefit large numbers of people throughout the world.

A. What I am saying is that while I accept the trade-offs between benefits and other societal objectives, such as protecting the environment, are often implicitly made, I would not want to see some explicit trade-off where we say "We will lessen our degree of environmental scrutiny because there appears to be some effect on the competitiveness of industry."

505. It must now be accepted, and we have had very sound evidence to that effect, that there are many people alive and well today who would not otherwise be so had it not been for the biotechnology industry. At what stage do you say people should stop getting that benefit to fit in with what you say are priorities over and above the future welfare of the large number of mankind?

A. If I could turn that round—

506. No, I am not asking you to turn that round, I am asking how you see that priority because I want to understand more clearly where you are coming from.

A. I think there is a distinction or a difference in this debate between the pharmaceutical side and the other applications of the industry. On the pharmaceutical side, anything which has given benefit to people has also been through a very thorough safety testing system. I am not as familiar with that system as I am with others, because often these sorts of products do not really have environmental implications, but I do not imagine the safety or efficacy to the recipient, or the regulatory regime which has to be put in place to ensure that, would be relaxed on arguments that otherwise people would not be able to derive the benefits. The benefits accrue from the product once it has been through a certain standard of scrutiny and approval. Is that not correct? What I am arguing is that benefits from this technology can be realised once it has been through a certain standard of scrutiny and approval on its environmental implications.

507. With respect, you also said, as I understood it, you felt environmental considerations, so far as you were concerned, were of prime importance?

A. They are to me. I am not necessarily saying the regulatory system as a whole—

508. You said that?

A. Yes.

509. So what I am asking you or trying to understand is how far you take that argument in preventing the development of a biotechnology industry which may possibly, in some far away days, have a risk which is a worse risk than crossing the road but will give enormous benefits? Do you believe how you perceive environmental risks outweigh any other benefit to mankind, or do you believe there is a dividing line, and if there is a line how can we encourage development of that technology and explain to the majority of people who have your fears that in fact the advantages can far outweigh the disadvantages?

A. I think if there is a line to be drawn it has to be drawn by society as a whole. I would not presume it is for me to say exactly where that line lies between risking environmental damage and accruing benefits. That is not what the regulatory system is for either. That is a series of political judgments and debate which should be held in a political arena with a very wide range of contributors, in much the same way as there have been other debates about environmental protection; nuclear power, for instance, as to how far we want to accept a risk from a nuclear re-processing plant as opposed to accruing the benefits. That debate goes on in a political and not a regulatory arena.

Chairman: Thank you very much. I have found this discussion extremely interesting. If you want to amplify what you have said to us later on, we would be very pleased to hear from you.

Supplementary Evidence from the Green Alliance

On the subject of vertical regulation for biotechnology products and horizontal regulation for research, my view is that it may be a good way of proceeding if adequate risk assessment procedures can be incorporated in all relevant product clearance systems.

This is necessary because there may be considerations relevant to commercialisation or large-scale use of a GMO application that won't have been dealt with at the research clearance stage. The implications of widespread use of herbicide resistance in beet is often cited as an example.

Shifting consideration of products to product clearance systems does not necessarily mean less administration. Adequate environmental expertise is needed within product clearance systems. This either means duplicating it between different procedures or passing consideration of environmental aspects back to a central committee. The latter is effectively what happens with the present system of horizontal regulation.

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HOUSE OF LORDS SESSION 1992-93

MINUTES OF EVIDENCE
TAKEN BEFORE

THE SELECT COMMITTEE ON SCIENCE AND TECHNOLOGY

(SUB-COMMITTEE II REGULATION OF THE UK BIOTECHNOLOGY INDUSTRY AND GLOBAL COMPETITIVENESS)

Thursday 6 May 1993

SENIOR ADVISORY GROUP BIOTECHNOLOGY

Mr B Ager and Dr K Baker

BIOINDUSTRY ASSOCIATION

Dr R Coleman, Dr L Nisbet and Dr R James

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THURSDAY 6 MAY 1993

Present:	
Hilton of Eggardon, B.	Renwick, L.
Howie of Troon, L. (Chairman)	Wade of Chorlton, L.
Perry of Walton, L.	Walton of Detchant, L.
	Whaddon, L.

Memorandum by the Senior Advisory Group Biotechnology

Examination of witnesses

Mr Brian Ager, Director, and Dr K Baker, Director, Biotechnology Science and Policy, Monsanto Europe, and Chairman, Strategy Committee, Senior Advisory Group Biotechnology, called in and examined.

Chairman

510. Good morning, gentlemen, and thank you very much for coming. I wonder if we can open the proceedings by your saying who you are and telling us a little bit about SAGB, and if you wish to make a short comment on your general attitude towards our enquiry, we would be interested to hear it?

(*Mr Ager*) Thank you very much. My name is Brian Ager. My interest in biotechnology stems from being Director of the Senior Advisory Group on Biotechnology, which is a position I have held for the last three years. The other relevant parts of my background are academic, as a biochemist. My experience also includes ten years in the United Kingdom Health and Safety Executive, first as a specialist inspector of microbiological and biotechnology issues and then as Secretary to the United Kingdom's Advisory Committee on Genetic Manipulation. I have also served with the European Commission's Directorate General for Science Research and Development and with the OECD as a consultant on biotechnology regulations. If I may, my Lord Chairman, give a few remarks by way of introduction of SAGB and its objectives, the group was founded in 1989 as a high-level industrial policy forum for debate and dialogue on the policy issues facing the application of biotechnology in Europe. Its current membership is 30 companies, both large and small, from the range of industrial sectors making use of biotechnology as an industrial tool. If I can summarise the overriding policy concern of the Group, it is to ensure continued growth, prosperity and jobs through European competitiveness in applying biotechnology. The SAGB has made very public its basic concerns and issues and it believes that the community can only benefit from biotechnology through active and competitive participation in research and development and production and marketing, and in order to achieve this we need an overall supportive policy climate for biotechnology in Europe. We know, of course, that the Community is going through many changes. Its operation is not perfect and we see this to be particularly true of regulatory structures in the area of biotechnology. I would also like to mention two other points concerning SAGB and relationships. In the context of this overriding policy concern, we have made considerable efforts to ensure a cohesive industry approach in this area and there are two particular initiatives that I would like to mention. First, there is the Forum for European BioIndustry Co-ordination, the FEBC. This is a new group of European industry sector federations, those that are concerned with biotechnology, which has been established to strengthen the existing co-ordination links between those federations and to provide an important forum where we can have an exchange of views and information. The creation of the Forum reflects the fact that biotechnology is increasingly being used by those particular sectors rather than constituting an industry in itself, and this, we believe, is consistent with the calls from SAGB and the European federations for a sector-based approach to regulations rather than a technology-based approach. The second initiative is the International BioIndustry Forum or IBF, which was set up in 1990 to share information and co-ordination of issues and principles common to the worldwide development of this technology. Here the principal associations are the SAGB in Europe, the Japan BioIndustry Association and the Industrial Biotech Associations of the United States and Canada. My point is that the SAGB works closely with both these groups to ensure a consistent and coherent industry position.

511. Thank you. Dr Baker?

(*Dr Baker*) Thank you, my Lord Chairman. I am Ken Baker and I am actually located in Brussels. I am Chairman of the SAGB Strategy Committee, which is a group of around 30 senior executives from the member companies of the SAGB who regularly give up their time and effort to work on the objectives that Mr Ager has laid out; in other words, to establish conditions in Europe such that we as companies can participate in establishing businesses and creating employment and actually contribute to economic and social improvement. By way of background, I have a doctorate in chemistry. I spent some time on a post-doctoral fellowship at Cambridge, where I worked with the teams at the MRC who were still at that time following on from the work of Watson and Crick. In fact, Crick was still there and that is where my interest, if you like, in this technology was first sparked. That was the late 1960s, I am sorry to say! I am also Director of Public Policy with Monsanto in Europe and our headquarters are also established in Brussels. About 25 per cent of our global business in manufacturing is in Europe and particularly in the United Kingdom, and frankly, we would like to keep it that way or even grow it through application of this technology. Much of our production is exported ex-Europe, so we have a particular interest here. Within Monsanto my responsibilities over the years have included research, business development, venture capital, public policy and, most importantly for this exercise, biotechnology policy. Perhaps I should also say that being located in Brussels over a period of

[Chairman *contd.*]

some 20 years on and off has given me an on-the-spot opportunity not only to observe and participate in the construction of the new Europe but also to see at first hand where the problems lie. I very much appreciate the invitation to come here and answer your questions.

512. Thank you. I would not worry too much about the late 1960s if I were you. I quite enjoyed them! I wish they were still with us, to be quite honest. However, be that as it may, you are, of course, a trade association and your concerns are how regulations and things affect your member companies' profitability and continued success, and other concerns such as the impact on the public and so on are perhaps less important in your eyes?

(*Mr Ager*) I think "trade association" is perhaps difficult but in terms of intention I think we are more of a policy forum—that is how we describe ourselves—where senior executives from these companies can get together and decide what they feel collectively about a particular issue. We are not there in the sense of being a trade-promoting organisation.

513. You are not?

(*Mr Ager*) No.

(*Dr Baker*) If I might add to that, as a policy forum one of the things we had wanted particularly in this area to do as an industry was to ensure that regulations were consistent with some sort of policy and in this particular area originally there had been no policy, so regulations, if you like, just grew like Topsy. That is one of the problems, as we see it.

514. Arising from what you have just said about regulations growing like Topsy, can you tell us how the EC Directives on contained use and general release evolved? To what extent were there consultations and to what extent were you involved?

(*Mr Ager*) If I can take the first go on that, they were, of course, evolved originally as a Commission proposal in the middle of the 1980s, coinciding with the end of the major OECD study on genetic engineering safety which began in 1983 and finished in 1986. I think that is important because there were a lot of discussions going on between Member States' experts at that time on the best approach, the way forward. The Commission proposal was then put forward to Member States, at first in a fairly selective and I would say ad-hoc way, for their views on whether this was a viable proposal, and the thing grew up in stages like that. From the point of view of SAGB it did not exist at that time so there was no input from this organisation *per se* and from my perspective at that time as being in Government circles rather than industry, so I cannot really add much to how industry was consulted or if it had been.

515. I wonder if Dr Baker can help us on that?

(*Dr Baker*) Yes. Let me try and recall the period, which I believe was 1987-88, if I recall correctly. I suppose the consultations, if there were any—and I am particularly looking from the Brussels perspective—were in the absence of any requirement on the part of the Commission who were drawing it up to have any transparency or consultation with industry or anybody else for that matter, and what went on is best described as being somewhat secret and selective, I guess. Perhaps I should say this. You can only make comments if you know that a Directive is being developed. We were not in the position of knowing when, how and where these Directives were being developed at the time eventually to come forward as a proposal to the Member States from the Commission.

516. So they appeared spontaneously from somewhere, did they—some new form of life?

(*Dr Baker*) It is very difficult to lay any light on that, because one was not part of the process. As I said before, if it is being deliberated within the Commission itself, within the Commission services, as an exercise, if there is not some intimation to the outside world that that is happening, then you are not in a position to comment.

Lord Renwick

517. Dr Baker, surely the relevant experts in the United Kingdom Department of Trade and Industry were involved, but was the industry not involved, through our Department of Trade and Industry and similar departments throughout the rest of Europe, with the Commission?

(*Dr Baker*) I cannot answer for the United Kingdom, because I am not based in the United Kingdom. Perhaps Mr Ager can respond to that. However, I can make a response for the case of Belgium where we are located. At the time that the Belgian authorities were requested for an opinion and they in turn came to *us* for an opinion, the Directives were at the very late stage of development. In fact, one was at the point of trying to chip away at something which was already constructed.

518. Obviously since the formation of SAGB in 1989 one of the objectives of the SAGB is to impact at a slightly earlier stage in the development of new Directives or later Directives, or to change the current Directives?

(*Dr Baker*) Perhaps I could hand that over to my colleague.

(*Mr Ager*) Yes, certainly we are in the business now of trying to comment on Directives which we know to be coming down the line. We are commenting on these Directives which we are talking about here and participating in what are called "simplified procedure processes" which are aimed at trying to reduce some of the bureaucracy around those Directives. So certainly we are active in that area there, and also with the European trade association groups, the federations which I mentioned earlier on, so that we can generally speaking get our act together and decide what we do think before talking specifically about their impact on pharmaceuticals or agrochemicals or whatever else it may be.

Chairman

519. There seem to be three aspects. There is comment which you have just mentioned, there is consultation and there is negotiation. We can see that each of these has an increasing strength, as it were. How far down the line are you in terms of negotiation with regard to these Directives?

(*Mr Ager*) I do not think we are in a position of negotiation on these Directives. I think we are in a

[Chairman *contd.*]

position of trying to get cohesive industry input on the development of the Directives.

520. You do not negotiate with the British Government, with Whitehall?

(*Mr Ager*) No.

Chairman: You comment.

Lord Walton of Detchant

521. It has been suggested to us that the experts from the Member States made certain recommendations before the particular Directives we are discussing were introduced by the Commission, but that those Directives, we understand—and we would be grateful if you could comment on this, though you may not be able to do so—were subsequently modified through the influence of the European Parliament perhaps affected by the attitude of various environmental lobbies. Have you had any evidence to suggest that this is the case?

(*Mr Ager*) Can I divide that into two, if I may. The first point is that from my personal experience I can certainly say that during the very early phases when we were being consulted or various people in Europe were being consulted informally there was a lot of advice against the approach being taken, and I would say that that was not followed in much of the Directives which you now see. The second issue is that when the Commission finally signs off on the proposal and it goes to the Parliament, yes, of course it is open to a considerable amount of debate, discussion and influence politically from all around the Community. There you will see that there will have been detailed comments and proposals on the Directives which were not necessarily positive, and that then gets put into the process which goes to the Council for final negotiation. I hope that that answers the question.

(*Dr Baker*) Perhaps I could follow up those same questions, my Lord Chairman. One of the comments you often hear, in Brussels in particular, from the academic community is that they were consulted but that their advice, particularly on the science of these Directives, was not included in the construction (if I could call it that) of the Directives themselves, which resulted in essentially a Directive in this case which is applicable with great difficulty when it emerged from the Commission. To come to the question of the Parliament, the Parliament, as you know, has to comment on the Directive as written, so it is working with something which is not particularly good to start with. I really do not think that the Parliament has made it any worse, so to speak, if that was the question, but I do not think it was improved, because it is very difficult to do that with this structure.

Chairman

522. So there is really very little point in your organisation trying to lobby the European Parliament rather than the officials; is that what you are telling me?

(*Dr Baker*) The SAGB's organisation at the beginning was to try to get a policy framework, a direction, if you like, within which regulations should be included. It was perfectly obvious at the stage that the SAGB was formed in 1989 that the Directive was well on its course to approval, if I can put it that way, and would have been extremely difficult to remove at that stage. The issue, as we saw it, was therefore to construct the proper framework within which such regulations should operate. In fact, the Deliberate Release and Contained Use Regulations are *not* the only regulations pertaining to this area.

Lord Whaddon

523. Apart from the influence of environmental lobbies, were there any other interest groups which have an input which influenced the Directives, as far as you know? I am thinking of certain areas where I do know there was a religious input. Were there any such bodies or any other bodies?

(*Mr Ager*) I am not aware of that.

(*Dr Baker*) No, I am not aware of that, except perhaps selected industry groups. I do know that various environmental groups made comments on various aspects. I am not sure that they had significant impact.

524. I come back to where did it come from, then?

(*Dr Baker*) It essentially came from within the Commission services.

525. Could you expand on that? What are "the Commission services"?

(*Dr Baker*) In this particular case—correct me if I am wrong, Mr Ager—it was DG XI which is the Environmental Directorate of the Commission, assisted by DG III which is or was the Industry and Internal Market Directorate, and individual experts within the services themselves who drew up the Directive. You will know, I suppose, in institutional terms, that the power of proposal lies with the Commission, and the proposal itself was drawn up within the Commission services.

Lord Renwick

526. Following on from the Directives, of course, there are the regulations laid down by each of the 12 Member States. Obviously your organisation is very much involved in this, or you get a feedback from your members who presumably cover the 12 Member States. Could you elaborate on the difference in the regulations between the various countries, which countries *are* regulated and which countries are much less regulated?

(*Mr Ager*) Yes, you are quite right, we do get feedback from our member companies as to how these Directives are being implemented in each of the Member States, or not, as the case may be. I think one would like to see a level playing field, as they call it, as an end result of that, and the feedback which we get is that it certainly is not a level playing field, there is a great disparity between the way it is being implemented in each of the Member States. I do not know whether Dr Baker may be able to expand on that in the context of Belgium particularly as an example, but certainly we do not get the feeling that they are being applied in a consistent and even-handed way.

527. Is it part of SAGB's policy as a policy forum to influence the position in individual Member States

[Lord Renwick *contd.*]

or really just to give strength to your members' arm in their own battles, as it were?

(*Mr Ager*) I would categorise it more as in the last category, given the strength of their arm. Our main focus is what is happening in the European context in terms of industry, rather than focussing on any national position *per se*, but of course the two positions are linked and one thing leads to another.

(*Dr Baker*) Perhaps I could expand on that a little. There is a significant unevenness in the implementation, or at least I should say the attempted implementation, of these Directives because they have surpassed by nearly two years the date for implementation in most Member States. The field is rather rocky; the level playing field is rather rocky. The Commission actually held a seminar on the subject at the end of September last year in Brussels. It was a public seminar to discuss the implementation and it became perfectly clear at that seminar, where each of the Member States presented their actual progress towards implementation, that there was a significant variation in the way in which they were being implemented. Coming back, Mr Ager mentioned Belgium. Belgium, for example, has attempted to implement these Directives vertically, that is to say, within the sectors that are concerned, simply because they saw that there were significant problems in doing it in any other way, not the least of which being the cost for a small country to set up a bureaucracy to handle such matters, so it was a question of cost effectiveness. That is the direct experience.

Chairman

528. I taken it then that your view is that the playing field is rather like the famous football field at Yeovil, where one set of goalposts is 9 ft higher than the ones at the other end!

(*Dr Baker*) There is no single market in a sense.

Lord Renwick

529. Could I follow up from Dr Baker's reply and ask if the SAGB identify any dangers, or potential dangers, in the lack of regulation in certain countries?

(*Mr Ager*) Do you mean dangers in the sense of risk or—

530. Risk?

(*Mr Ager*) As a general response I would say that we believe that we need adequate regulation on the Science Base and that will escort products from the laboratory to the marketplace, and if there is inadequate regulation which is not appropriate, yes, there would be a risk in certain circumstances but it is not a risk which is related to biotechnology *per se*. I would suggest it is the risk to traditional use of classes of product, whatever they might be, whether it is agro-chemicals or pharmaceuticals or whatever else.

531. And, of course, your members would be responsible enough and sensible enough to act in a businesslike manner to make sure there was no risk and, therefore, they would not reply by developing a product that was not entirely safe?

(*Mr Ager*) Yes, I would say that.

Lord Walton of Detchant

532. May I follow up that point because it is clear from what you said that you favour in general vertical as distinct from horizontal regulation. You say in your written document: "One of the major catalysts for promoting biotechnology's competitive economic benefits is the structure of the regulatory system. Correctly structured, the system will both encourage and ensure safety—wrongly conceived it will stifle growth without adding to safety." That is a clear statement of your policy. Does it, therefore, follow that you, as an advisory group, would wish to see significant modification in the existing Directives?

(*Mr Ager*) Yes, I think that is a fair comment.

Chairman

533. Do you think there is any likelihood of this happening?

(*Dr Baker*) Perhaps I could answer that. One of the things the SAGB has done is to encourage the Commission to develop a Community policy for biotechnology. That they have done and there is what they describe as a communication which issued on the subject in April 1991, again nearly two years ago. Within that communication there is a statement which says that all regulations must be reviewed, in other words, that there must be a look taken at the existing situation and, in particular, the questions of horizontal and vertical and adaptation of technical progress. Having said that, the progress to review is somewhat slow. Requests to participate in a dialogue to encourage that process by the SAGB to the Commission have been treated with a good deal of slowness in terms of response. It is extremely difficult to get the process operating, but I should say that the Commission has recognised that there needs to be a regulatory review.

534. If the regulations were to be changed how would you like to see them changed from the Directives that the regulations seem to come from?

(*Mr Ager*) We would work on that in terms of detailed requirements, suggestions, proposals, whatever we might call them, but I think in an outline sense I would draw your attention to some of the written evidence, where at the back here we gave three comparison tables which indicate how we see the regulations in the United States, Japan and Europe, and we used the term "untangle" when we, the SAGB, met Vice-President Bangemann last year because it seemed to us that summed up very nicely the need to untangle the horizontal from the vertical and allow us to come back to a straight-line path that escorts one class of product from the R&D stage to the marketplace. That is what I believe the charts tried to put across. That is in general terms what we would like to see. In specific detailed terms, we are working on some proposals we would like to put forward to the Commission following our meeting with them at the end of last year.

535. These are detailed amendments to the existing Directives, I take it?

(*Mr Ager*) Yes, that is correct.

(*Dr Baker*) It could very well turn out that the detailed amendments will not be sufficient to achieve the objective. Going back to the question itself, one

[Chairman *contd.*]

of the industry's intentions, or at least desires, would be to reduce the bureaucracy and increase the certainty of getting an answer from the regulatory process, and particularly the question of uncertainty. When you are making an investment decision the last thing you want is uncertainty as to where you will be able to apply whatever it is you are doing. That substantially affects the decision on the making of the investment in the first place.

Lord Perry of Walton

536. I would like to ask a question about the European regulatory system as you have it laid out here because it seems that the Contained Use Regulations, which affect all things like drugs and pharmaceuticals, are actually controlled by DG XI, whereas the non-GMO products are DG III. Is it necessary for a Member State which is implementing these regulations to so divide because it would be perfectly possible, would it not, for the Health and Safety Executive, for instance, to run the horizontal control in protecting the workforces, but it would be equally possible for the contained use of pharmaceutical products to be handled not by the Department of the Environment, which would be parallel to DG XI, but by the DTI? Is it possible for that to be changed by Member States?

(*Mr Ager*) Can I have a first go on that. I believe, my Lord Chairman, yes, it is possible for Member States to do that, although I am not in a Member State's government any longer, but the key point, I think, to us is that we have to be aware that by constructing a European Directive that focuses as its regulatory trigger on a technique, even if you then carve that up and put it into the right place when you come back to London, Paris, Bonn or wherever else, you still run the great risk of introducing discrimination against that technique and getting out of consistency (if I can put it that way) with the way you would normally handle those risks. It is not just a bureaucratic carve-up, it is the fact that the Directives themselves are triggered by a technique and not by a risk factor *per se*. I do not know whether that is a very clear answer.

Lord Perry of Walton] I did not quite follow it, but okay.

Lord Renwick

537. Mr Ager, we have heard some evidence on the activities of the Department of Trade and Industry Deregulation Task Force and I wondered if you would like to tell us of SAGB's involvement with it?

(*Mr Ager*) In fact, no direct involvement. We send them the material we produce obviously; we keep them informed as we do other people in Member States' governments, but we have had no direct involvement with the task force.

538. They have not a committee on biotechnology specifically or the regulation of it?

(*Mr Ager*) Not as far as I know, but I am not sure.

Chairman

539. I think that Dr Baker wanted to add something in reply to the question by Lord Perry, am I right?

(*Dr Baker*) Yes indeed. Lord Perry, you said that you did not understand the response. Perhaps I could try to give an answer through experience. I shall come back to the case of Belgium again which is attempting—because the Directives are not yet implemented in Belgium—to implement them such that the Agriculture Ministry would look after those questions related to agriculture. You raised the question of contained use there. That properly rests, or should properly rest, with the structure which is in place to carry out inspections in reality, so that would be, I believe, the Inspectorate of Factories or something of that sort here; it is part of the HSE. That logically fits into that organisation. Now step back a bit. Perhaps I should say that in the United Kingdom and in other Member States there *do* exist structures which can accommodate these Directives in a vertical fashion, if they have been developed correctly. The problem was that the Community, in Community law, did not have the same framework Directives, as they would call them, which could accommodate such Directives. There is no framework Directive for food, there is no framework Directive for the environment, etcetera. So there was no structure in which these could be put. The structures existed in the Member States, but not at Community level, hence the problem.

(*Mr Ager*) Perhaps I can add that there is one exception to that, my Lord Chairman, and that is the framework Directive on Health and Safety at Work which has been in existence for some time now from DG V in the European Commission. That framework Directive allows them to hand on daughter Directives on asbestos, noise, benzine, biological enzymes and whatever else at work. It is a logical construction similar to the Health and Safety at Work Act which exists in the United Kingdom.

540. We have spent a great deal of time on these regulations, which is quite proper since they are a great concern of yours. I wonder if I can ask you something about the effect of them on your member companies. Is it possible that the regulations and Directives as they stand have led member companies to make strategic business decisions which they would perhaps have preferred not to make?

(*Dr Baker*) Perhaps I could take up that one. I think the response in terms of what is happening in Germany is fairly well known—that there are many German companies who have moved either to the United States or Japan. We, as the SAGB, would not necessarily know what decision-making was going on within a company with respect to its decision-making as to the location of a particular investment probably until it has actually happened. Anecdotally, I can tell you that within my own company, Monsanto, it is the perceived climate for an investment which is very, very important. When the question of a biotechnology-related investment comes up, whether it be a research which is still an investment or a manufacturing investment, I have a very difficult time in Europe arguing against what is perceived to be the negative climate. One is pushing uphill, in a

[Chairman *contd.*]

sense. So it is more than the regulation there; there is perceived to be a negative climate for investment in this technology.

541. Monsanto, if I remember rightly, had a place in Ayrshire at Dundonald, did it not?

(*Dr Baker*) I believe you are talking, my Lord Chairman, about the textiles factory.

542. Am I? Then I can stop, and I will! Carrying on on the lines of the previous point before I diverted myself, there are, of course, a number of other factors—and you have hinted at those—in the strategic decisions which businesses make. Would you think that the regulatory climate or regime would be an important one of these, or would it just be one amongst the rest, of no greater significance than any other?

(*Dr Baker*) Perhaps I could answer that. The sort of factors which you would consider would be the tax structure, the competitiveness, the worker productivity, perhaps social structures, the availability of an educated workforce and so on and so forth, in addition to the regulations. As I said before, it is important that there is regulatory certainty, that you know that you are going to get approval to do whatever it is you are going to do and that there will not be changing of the goalposts during the time you are attempting to make your decision. There is a perception, as I have just mentioned in answer to the previous question, that there is a negative political climate, amongst other things. Therefore, in Europe the regulatory aspects take on a far greater importance than they should do.

543. So they do have greater weight than you might expect?

(*Dr Baker*) Indeed.

Lord Wade of Chorlton

544. In everything that you say you seem to be expressing a concern that there is not the right opportunity or no proper structure for you to be able to give business and the industry suggestions and input before the Directives are formed. You have given your recommendations on what your views on the Directives would be. I would like to know what your recommendations might be to make the system more clearly open, so that both the industry and anybody else who has any other views on biotechnology has a clear method by which they might express their views before the Directives are formed or after they are confirmed, and how any influence might be brought. There seems to be a wall between what anybody who has views on the Directives might want to input and the actual system of getting them into the deciding process. What is your answer to that?

(*Mr Ager*) Perhaps I can just make a few general remarks there. One of the constant pleas from SAGB since it began has been for more consultation and transparency on exactly that point of what Directives are being cooked up inside the Commission and how does one get a chance to say something about them before it becomes too late. It has been a constant plea from us, I think, from the beginning. We have some papers which we would like to offer you as leave-behinds. One of these contains a list of proposals which *we* are aware of which are currently coming up inside the Commission. Again, the concern remains the same that can we get a chance, along with everybody else, to say what we think about these, and what is the opportunity to do so. There is no formal structure for us at the moment for doing that.

545. So that you *would* be advising that there should be a proper formal structure established within the European Community and within the various groups to have some kind of consultancy process; is that what you are saying?

(*Mr Ager*) Certainly an effective structure, whether it is formal or not.

546. Have you any very clear recommendations that you would like to put forward, though, as to how that might work?

(*Dr Baker*) Perhaps I could respond to that one. This problem is not unique to biotechnology or development of Directives for biotechnology; it is equally applicable to any Directive which is being developed by the Commission. It is also related—I hate to say this—to the Maastricht Treaty. It is also related—I hate to say this—to the Maastricht Treaty and the question of how open should be the Community structures and in particular the Commission. I notice in this morning's *Financial Times* that there is a proposal that has been tabled by the Commission yesterday (I believe it was) for more—it is described as openness and access to Community documents as they are being developed. That is something that we would support and, in fact, goes on along with the process that should be in place. In a sense I do not think it is open to industry necessarily to suggest the process. That has to come from the other side and, in fact, is doing so. Whether it will be efficient is another question.

Chairman

547. We are beginning to run out of time. I have one question to ask. We will make this the last one unless any of my colleagues have something specific they want to ask. You put out a report called, "Economic Benefits of European Competitiveness" and you gave some figures for the future market impact of biotechnology. Another report from CEST suggests that biotechnology will only add 0.15 per cent. to United Kingdom annual growth. Are your figures over-optimistic, do you think?

(*Mr Ager*) May I have first go on that. This is a report which we produced in 1990 and we were looking there at the projected market impact of biotechnology in various sectors. I think there are two points to make. First of all, they are estimates based on our getting our act together in Europe and getting it right. Secondly, because this is an enabling technology that is pervasive and goes through every part of R&D to production, it is very difficult to get a clear definition of exactly where biotechnology is in that kind of process. I would say that in any event precise figures are probably not possible but the overall impact, or potential impact, is clear. Secondly, we have had an SAGB poll recently of our member companies, looking at where they intend to invest in the future compared with what they invest now, and I would like to leave that behind for you, if

[Chairman *contd.*]

I may, because it has some interesting figures on their intentions in a worldwide context, the United States, Japan and Europe.

Chairman] With the observation that the way the economy has been going lately and with the kind of growth we have been having, I would have thought 0.15 per cent. was quite a reasonable figure, thank you very much for your attendance. You will get an opportunity to look at your replies and perhaps modify them or correct them, if you feel they need correcting and working on in future. Thank you very much indeed, it has been a very interesting session, to me at any rate.

Memorandum by the BioIndustry Association

Examination of witnesses

DR R COLEMAN, President, BioIndustry Association, DR L NISBET, Chief Executive Officer, Xenova, and DR R JAMES, Managing Director, Pharmaceutical Proteins, called in and examined.

Chairman

548. Good morning, gentlemen. I wonder if you would care to identify yourselves and say a little bit about the BioIndustry Association?

(*Dr Coleman*) Yes, my Lord Chairman. My name is Ron Coleman and I am the President of the BioIndustry Association. I am accompanied by Dr Louis Nisbet, who is the Chief Executive Officer of Xenova, and Dr Ron James, the Managing Director of Pharmaceutical Proteins, both members of the BioIndustry Association. The BioIndustry Association is a trade association. We represent approximately 150 companies in the United Kingdom and there are another 80 companies in associated organisations with which we work. Our basic mission is to try and help develop a good climate for the commercialisation of United Kingdom biotechnology. If I may, I would like to say a few words by way of introduction. We have sent you a written memorandum but there are a couple of points I would like to highlight. First of all, I am very pleased that you have linked regulations with competitiveness because too much of the discussion on regulations in the past has been carried out one might almost say in a vacuum as far as competitiveness has been concerned. Biotechnology is the use of biological agents to make products and services. There are already significant revenues being earned from that and these are increasing very rapidly. In the United States it is currently of the order of $8 billion a year and in the United Kingdom it is of the order of $600 million a year. The growth rates are of the order of 20 to 30 per cent. per annum, so by the end of the century, something like £90 billion of world sales will depend upon biotechnology. This is potentially a very significant change from where we were in the 1980s and even where we are now. The United Kingdom is extremely well-placed to win in this market. We have first-class companies in the areas which tend to use biotechnology, such as pharmaceuticals, chemicals and food. We have large numbers of new, small companies, something like 100 in the United Kingdom—more than anywhere else other than the United States—which are exploiting the developments coming out of the Science Base. We have an excellent Science Base in this area in the United Kingdom, second in absolute terms only to that of the United States, and many of the major discoveries in science which underpin biotechnology were made here. So there is no reason why the United Kingdom cannot continue to succeed and have a significant share of this world market. One thing that could damage this, and damage it seriously, is the Government, the Commission and the regulatory environment. I am not here to ask for hand-outs but what we are asking for is that people consider the industrial impact and perhaps have some kind of cost compliance assessment when they are developing regulations. One of the problems I see at the moment is that there is a lack of leadership in biotechnology in the United Kingdom Government. About ten years ago, sitting in one of these very rooms, Patrick Jenkin asserted that the Department of Trade and Industry was the lead Department for biotechnology. That was a great help for a few years but that leadership role has been either diluted or forgotten recently. If one is really concerned about competitiveness in industry, DTI should either be given or re-assert that role and then it would have a significant impact on the way regulations were formulated and implemented. Too often industry spends its time looking at dreadful drafts which come out, totally unable to be implemented and, therefore, needing serious modification. It should not be the job of industry to do Government's job for it but it has to at the moment and, of course, when you are always starting from something which is poor it is very difficult to make it perfect. All you can do is make the best of a bad job.

549. I think it was Bismarck who said that politics is the art of the next best thing! Is it perfectionism that is perhaps going a little too far? Anyway, taking up one of the points you made in your statement just now, you are obviously worried about the cost of complying with the regulations and so on. Can you tell me, are the costs really significant, and, going on from that, in paragraph 10 of your paper you talk about compliance cost assessment. Could you say something more about that? You touched on it a moment ago but who would make it, for example?

(*Dr Coleman*) Who would make what?

550. Who would make the assessment? Would the assessment be made by the company involved or would the assessment be made by the Government regulatory authority or what?

(*Dr Coleman*) What I am really asking is for people to turn the clock round. When the environmental lobbies were concerned about industry they asked us to produce environmental impact studies. What I am suggesting is that before people regulate they think of what is the cost of compliance. So it should be the

[Chairman *contd.*]

regulators who do it and then perhaps get it checked with industry to see whether they agree.

551. So the regulator would try to assess the cost of the proposed regulations, much in the way that, if you look at the front of a Parliamentary Bill when it comes out, there is an explanatory page or two of the Bill and an assessment of the cost at the end. That is the kind of thing, is it?

(*Dr Coleman*) That is right, because in that way some of these things would never start if one realised how expensive it was going to be to implement.

552. This assessment presumably would have to be made in some form of collaboration between the regulator and industry, in order to get the figures right or wrong, as the case may be?

(*Dr Coleman*) I am sure that industry would be willing to provide data if they were asked for it.

553. Would not they tend to be on the high side?

(*Dr Coleman*) I do not think it is reasonable for you to assume that industry would be anything other than open and honest about it.

554. I was not trying to be reasonable, I was trying to be cautious! Thank you. We have a fairly strong feeling, I think, that most industrial witnesses would prefer some move away from horizontal to vertical regulation. I take it that you agree with that. Would it be easy to make that change?

(*Dr Coleman*) Not only do we agree with it, I think it would be highly desirable and not very difficult. I draw your attention to our report. We said that "The US White House policy on regulation states: 'products developed through biotechnology processes do not per se pose risks to human health and the environment'." If you start with that premise, then you work in a totally different way; you then regulate the products, and it does not matter how the products are made, whether they are made using biotechnology or synthetic chemistry or natural processes, it is the products which must be safe, efficacious and of the right quality. We have a regulatory system in place which can do that at the moment.

Lord Wade of Chorlton

555. Dr Coleman, what you say from where you operate within the industry may well true, but there are an awful lot of people who do not believe it to be true. You have already said that you are concerned that Government does not give, if you like, the lead and the support of the technology to the industry which you believe it should. Surely you must appreciate that one of the reasons why it probably does not is that it is aware of strong feelings amongst many people that there *is* something to be concerned about in this field. How would you deal with that, or how does your organisation deal with the fact that there are in society large numbers of people who do not understand it and, because they do not understand it, are frightened of it and frightened of its possible influence on the future? We have had evidence to that effect. So that it is not just a question of Government changing its view. Government has to take into account all kinds of influences which are brought to bear on it. Do you believe that there is a role for industry to play in persuading people of the statement which you have just made, or do you believe it is a role which your organisation can play a greater part in, or do you believe it is something which Government has to do something about?

(*Dr Coleman*) The answer is that all three need to do something: industry, Government and organisations like our own.

556. What would you believe they should do, then?

(*Dr Coleman*) First of all, I think one has to have some basic principles. In the case of regulations we believe they should be based upon sound scientific principles. We have had evidence in the past of regulations being introduced for social reasons. That is not a good reason for introducing regulations on a technology, for example, to ensure that small farmers in Germany are not put out of business. We do not introduce regulations to stop small businessmen in the Midlands being put out of business, so why should social implications come into this? There are other ways of dealing with those. As to this whole question of biotechnology being dangerous, there *are* potential dangers in a few specific instances. If you are using pathogens, clearly you have to protect the worker, the environment and everyone from them. However, most of biotechnology is perfectly harmless, and people do not seem to understand that.

557. The point is, though, that you do not have to convince me, you have to convince an awful lot of people out in society who do not agree with you.

(*Dr Coleman*) I accept that. I can tell you the things that *we* are trying to do. I have produced a list here—or it has been produced for me—of things which we are doing to try to address this issue of what is often called public acceptance of biotechnology. We have held conferences where we have had a very wide audience, addressed by the Archbishop of York and other people of various kinds, to try to get a consensus. I think that that was very helpful. We have round-tables where we have brought together representatives of lobbies concerned with green issues, animal rights and so on, where we have tried to exchange information and have succeeded in exchanging information, so that if we have more information on both sides we can understand them and they can understand us. Those are the kinds of things which we have been doing and will continue to do. However, it *is* a problem which requires substantial resources. Any of you must be aware of the vast amount of money which is spent on advertising to get people to buy a particular product. One is not going to change public perception without spending significant resources. So we need somehow or other to pool our efforts within Government and within the industries, to try to make this happen, rather more than we have at the moment. We are not blameless.

Lord Walton of Detchant

558. May I go back to one point which you raised earlier. I shall be interested to know whether, in relationship to Government, you have had any input into the work of the Office of Science and Technology, and whether you have had any input into the forthcoming Science White Paper. That is

[Lord Walton of Detchant *contd.*]

my first point. May I also raise the issue of public understanding, because in certain spheres of the public mind the word "biotechnology" is equated with genetic engineering and raises the spectre of genetic manipulation and other potential fears? You know and I know that the regulations protect the environment and human health very precisely as they stand at the moment. Not only did you quote the United States policy, but also the SAGB quoted the 1991 Japan Government White Paper, saying that there has *never* been any particular risk to the environment or to human health of biotechnology, including recombinant DNA technology. The question I am going to ask you is, do you have input into organisations like COPUS (the Council for the Public Understanding of Science), the British Association for the Advancement of Science and all the other organisations which are striving to achieve the same aims as yourselves, namely a much better public understanding and perception of what biotechnology means and what it can offer?

(*Dr Coleman*) Let me answer your first question first, because it will be short. Yes, we have submitted a memorandum to the Office of Science and Technology—one of very many they must have received to help them write their White Paper. On the second question, yes, we are aware of these other organisations, and quite frequently at the conferences and round-tables which we organise we try to involve them as well. One of the ones you did not mention which, for example, we have been quite active in is the Interest Group on Education on Biotechnology, because it is so important to try to ensure that people leaving school have a better understanding of biotechnology before they go out into the world. Yes, we do what we can, but we have a very limited budget.

(*Dr James*) Perhaps I can add something to that. The very fact biotechnology is regulated in a horizontal fashion suggests to the public at large that there is some kind of danger in biotechnology which requires regulation. If it were regulated in a vertical fashion—that is, if the products were regulated in the same way as they also are now—that perception would start to disappear and we could have, I think, some confidence that those people who govern and regulate us might either have a basic understanding of biotechnology or access to experts so that they would have the confidence that there *were* no risks and that indeed this was the case. All the while biotechnology is seen to be separately regulated the public and the media are entitled to think there is some danger which requires special regulation.

Lord Whaddon

559. What has been your input into the United Kingdom scene? Do you have any input into the European scene, the Commission in particular, bearing in mind their somewhat different approach to what others may have, either directly or through the Senior Advisory Group Biotechnology?

(*Dr Coleman*) There is another group in Europe, the European Secretariat of National Biotechnology Associations, and the BioIndustry Association has been working within that group to try and influence the Commission. Of course, we also know SAGB and we meet with them and would particularly, in the future want to help them more to understand the particular concerns of our members and have a more co-ordinated approach to Europe. One of the things I have recently done in a personal capacity is to write to the chairmen of the many organisations which are involved in biotechnology on behalf of the industry and suggest that we get our act together rather better. This hobby horse of mine, if you like, is being discussed at the moment but the signs are that we will be able to present a more coherent view from the industry on many issues associated with biotechnology in the future.

Lord Renwick

560. May I follow on on that, Dr Coleman, remembering your comments earlier about the need for an identifiable presence, shall we say, in the DTI, as there was when I believe Lord Jenkin was there. Have you made suggestions as to how that might come about and in what sort of form? Should there be a separate department within the DTI? I am aware of what Bismarck said but somebody else said, "There is no situation that is so bad that Government cannot make it worse"! That is rather flippant but how would you want the DTI to help your organisation and, therefore, your members?

(*Dr Coleman*) The organisation is already there. Under the President of the Board of Trade there was a re-organisation of DTI last July and there is a division called Chemicals and Biotechnology with a Grade 5 who in effect runs biotechnology in DTI. So there is a grouping already there. What is necessary is for other departments to recognise a first amongst equals, if you like, in this area of biotechnology, and this concept of a lead department is a very good way of doing it. It is quite common in government to have lead departments and if others would recognise that and, therefore, consult on these issues, and listen as well as consult, then we would have a much better situation.

561. It occurs to me, my Lord Chairman, that there is no parliamentary group which actually takes a direct interest in biotechnology. There is the Parliamentary and Scientific Society, of course, but that is very general and, of course, it comes under that. Would you agree with that?

(*Dr Coleman*) In a way it would be a disadvantage if people concentrated on biotechnology rather than the products and the services. As my colleague Dr James has just said, if you keep over-emphasising biotechnology people think there is something to worry about. What we are really interested in are the products that come out—the pharmaceuticals, the diagnostics, the foods, the seeds and so on. Those are what are important, not the technology. It is just an enabling technology. It is like information technology. You do not have a group worrying about information technology, I do not think.

Lord Renwick] In fact we do. I happen to be the Hon. Secretary of it!

Lord Whaddon

562. If there is a tendency for people to think in terms of biotechnology as a special problem, would it be wiser not to have a British BioIndustry Association at all?

(*Dr James*) That is like saying there ought not to be a chemicals society or a pharmaceuticals society. It is a branch of science like anything else.

563. So we could hardly avoid people regarding it as something special?

(*Dr James*) We could hardly avoid people regarding it as something different. Chemists may regard chemistry as being special over physics but not everybody would necessarily agree with that proposition, especially not the physicists. It is different but not special.

Lord Walton of Detchant

564. It is clear from what you have said that you wish to see the existing Directives relating to biotechnology modified. I think that is very clear, and you favour the vertical regulation?

(*Dr Coleman*) Yes.

565. In your paper you said that on the Commission's original proposal for the Contained Use and the Deliberate Release Directives you were relatively happy but the approach towards legislation of individual sectors of the biotechnology industry was changed during the process of negotiation in the European Parliament and the Council of Ministers. You go on to say that academic and industrial interests at a European and national level were systematically excluded from this debate. How can we or anyone take action to see that that does not happen again?

(*Dr Coleman*) It is very difficult to come up with a solution because what tends to happen is that you have a draft which you discuss and maybe get more or less agreement on, but then what happened in this particular case was that it more or less got hijacked by other interest groups who saw that this was a good away of protecting things which are not directly related to the industrial aspects of biotechnology. Of course, it then finally comes back to the Council of Ministers but biotechnology is then very small beer compared with the totality of issues which concern government. This is inevitably horse-trading on different issues and, "We'll let this go through as long as we get something else." So it is very difficult to see how industry can influence the process at that stage. Nevertheless, what we are concerned about is the United Kingdom's implementation of that Directive. That is within our hands.

Chairman

566. Could you tell us who the hijackers were?

(*Dr Coleman*) They were to some extent small farmers and to some extent animal rights people and that kind of organisation.

567. The social side, which we did not fancy too much earlier on?

(*Dr Coleman*) Yes.

(*Dr Nisbet*) If I may make a comment, my name is Louis Nisbet and I am Chief Executive of a company called Xenova Ltd, based in Slough, a little west of London here. My background and training is that I trained as a microbial biochemist in the laboratories of Sir Ernest Chain in the Imperial College of Technology, a bit closer to this House, and following that training I went into industry and received industrial training and gained expertise in pharmaceutical drug discovery and development with Glaxo, Roche and, in the United States, with Smith, Kline & Beckman (as it was then). What I would like to address is the fact that I think it is quite appropriate when one is going into a *new* situation that one should have concern about prospective changes. However, I think we need to remind ourselves and the public that we now have considerable experience in realising the benefits of biotechnology in the pharmaceutical arena with a whole host of proteins, monoclonal antibodies, vaccines, which are not only treating disease and saving lives but we have tremendous experience in the release of genetically engineered plants into the environment—avoiding Triffids or things like that! I would submit, that certainly in the case of the pharmaceuticals, they were subjected to the same rigorous analysis by the regulatory authorities as any other pharmaceutical product not derived from biotechnology. They have come through, they have performed well, safely, efficaciously, and their quality is very tightly and rigorously controlled, perhaps more so than more conventional pharmaceutical products. So I think we should comfort ourselves and the public with the fact that we have experience and we have tremendous benefits from this technology. We of course *do* need to look after the industrial interests and make sure the United Kingdom, with such a strong franchise in pharmaceuticals and other areas, is able to exploit this technology in a competitive manner with respect to products which will be sold worldwide and generate tremendous revenues in due course.

568. We were talking about the government departments a little while ago. I notice on page 13 of your paper you mention one or two things which you would like to explore with these government departments. In particular, you talk about the "VALUE" programme of the European Community and the extension of the Enterprise Zone system. I wonder if you could tell us a little more about these two things?

(*Dr Coleman*) Would you mind, my Lord Chairman, if my colleague Dr Nisbet put that in context? We are particularly anxious to talk to you about finance for biotechnology, and that is a part of it. Perhaps I could ask him to deal more generally with your question.

(*Dr Nisbet*) I think there are four other key factors I would like to touch on, but spend most of my time commenting upon the financing of young companies. The four factors, of course, are access to capital and the financing of biotechnology companies; secondly, technology transfer from academia to industry in a more effective way than we currently achieve in this country; thirdly, partnership within the United Kingdom or Europe between United Kingdom based and indeed European based biotechnology emerging companies and established multinational companies and what we do to foster that; then finally, the training and development people who are much needed to staff these new technology-driven companies. However, to concentrate upon the

[Chairman *contd.*]

capital side of things, even with the brightest ideas, the best people, the strongest technology, you cannot grow a business without access to capital. For example, a young emerging pharmaceutical company is likely to need somewhere around $200 million of capital before it can expect to generate revenues which would provide it with a break-even situation. That is based on considerable experience in the United States to date, and there is no reason to expect that the United Kingdom model should be any different at this stage. In the first place, we need venture capitalists to take major risks in setting up companies. It is a very high-risk investment that these people make. They have limited funds available with which to do this, and indeed they do need to assemble themselves considerable research skills to be able to judge those worthy investments from those which perhaps are not worthy. We certainly would like to advocate some kind of tax incentive for investments in nonprofitable companies whose expectations of entering profitability are likely to be of the order of an average 10 years from start to profitability. That is a very long time for someone to sustain an investment. Clearly venture capitalists cannot take companies all the way through, therefore I do think we also need to turn our attention to what I would call the pre-public phase of financing, the post-venture capital phase. In the United States of America the experience is that individual private investors and indeed institutions are prepared to invest large sums of money in companies somewhere between two and five to six years post their founding, when companies may be raising very large capital sums but not yet addressing the public market, not yet providing liquidity. In the United Kingdom we have a more limited base in one respect, and that is that there really is only one source and that is the institutional investors, people who hold our pension funds. We give them the money, why do not they give some of it back to us to establish our companies?

569. You would not want that money to go to a high-risk company, though, would you?

(*Dr Nisbet*) I would certainly wish some of it to go to some of those high-risk companies which were judged worthy of investment on the terms that the potential gain was considerable from that investment, and on the basis that the person making the investment would make not one investment but a number of judicious investments which would recognise that there will be attrition, but that there will be considerable growth in some companies which will more than offset the attrition which may be seen with some of them. So I think it is a matter of institutions developing again expertise and taking a portfolio approach. However, the size of the United Kingdom Public Sector Borrowing Requirement and its relationship to institutional cashflow is limiting funds for young companies. In the case of Xenova, we had the rather curious situation in December 1990 of raising £5 million out of a £7 million financing from institutions both in Scotland and in England, and indeed one from Japan. However, with much advance in the development of the company, considerable patents and other assets to demonstrate the success of our exploitation of biotechnology, just in 1992, and indeed through the year to December, we found that United Kingdom institutions felt unable to invest in non-liquid stocks, and the same institutions who gave us money in 1990 could not give us money, basically because it was a policy coming from the top of the institutions as a result of the cashflow requirements of those institutions. As a result of this we and, I have to say, a number of other young companies are having to seek capital elsewhere. Xenova was very, very successful in raising capital. We raised $32.3 million largely overseas. I think it is a travesty that we had to go overseas for that money, because the growth in that money will therefore go back overseas. So I think we need to do something about this to encourage institutions to invest in illiquid but more developed young companies beyond the pure start-up phase. Besides Xenova there are also similar experiences at Pharmaceutical Proteins, and Cantab Pharmaceuticals, for example—

570. I do not think we need too much detail at this point.

(*Dr Nisbet*) Very well. Then the last point I would want to make is about the London Stock Exchange and the moves we see there, which we do welcome, to make it possible for young development-stage companies without a so-called adequate record to list. Indeed, we would advocate a greater move towards the American way of handling the flotation of young companies, and that is that we should be relying very much more on full disclosure and self-regulation by the companies and, of course, a review of their documentations by the London Stock Exchange. Indeed, investment in liquid stocks does truly need to be market driven and driven by the appetite for an individual company against a basket of possible investments. We have too few eggs in that basket right now, recognising all the points of pressure. I think that perhaps I should stop there.

Lord Renwick] My Lord Chairman, can I very quickly comment on what Dr Nisbet has just been saying. I think he has been relating a saga which has been very well known to all of us, to everybody in industry, over the last 10-15 years or since whenever. We have a particular form of investing system in industry which is necessarily directed towards short-termism. Our banks operate differently to those in Germany, in that they take a more arm's-length view than they do in Germany. I congratulate Dr Nisbet for being able to go internationally for funding. Unfortunately, shareholders do like dividends, and if you are going to wait for 10 years for a return on your investment, my goodness that is one big investment and it has to be balanced by something which is going to produce income. However, I do see your point. But I also take Dr Coleman's point of view, my Lord Chairman, on how the Science Base is good in this country in this case and I am glad to hear him say that. I also see in Appendix 1 of your paper—I have not been able to count them but there must be 60 or 70 companies that have started up since 1980 and obviously they are all in there for their share of investment funding from someone, so some of them, I am sure, will be succeeding. It is the very large companies, of course, in the pharmaceutical industry where we do excel and have very large capital bases. There is an enormous investment and with smaller

[Chairman *contd.*]

companies it has always been a problem. When I go to a project they always tell me there is much more money looking for really credible projects, but then I am not giving evidence to the Select Committee. May I apologise, my Lord Chairman.

Chairman

571. Thank you very much. I must say I am a little surprised that Dr Nisbet was able to find all these Scotsmen who are going to wait for ten years to get their money back! They could not have been in Aberdeen!

(*Dr Coleman*) Before you close, my Lord Chairman, Dr James would like to mention one other particular aspect which we think is of particular significance if we are going to develop our technology.

(*Dr James*) This is an area which does affect investment, and certainly affects our ability to compete globally. It is the situation with regard to patents in biotechnology and specifically those which relate to animals and living organisms. Here, I think, if there is any way to resist the idea that there should be a social component or a moral component in the decision as to whether something is patentable or not, it should be resisted. I am not saying social and moral decisions ought not to be made. What I am saying is that the Patents Office and the patent system is certainly not the place where those decisions ought to be made, and that people do not make investments unless they believe there is an opportunity for the company to succeed. If it is unable to protect its technology it cannot succeed.

Lord Walton of Detchant

572. I feel I must make the point that there is a strong feeling in certain quarters of the medical profession that it might be thought improper, for social or moral reasons, to patent a form of gene therapy that could help individuals suffering from inherited disease worldwide; but that is not, I think, quite the issue you were addressing?

(*Dr James*) It is not the issue I was addressing. I was addressing the question of whether there is an invention there or not, and whether it should be patentable only because it either *is* or *is not* an invention.

Chairman

573. This dialogue could go on for the rest of the day. We will wind it up there. If you wish to augment the information you have given us by more detail, especially on patents, for example, we would be very pleased to hear from you later on. Thank you for coming.

(*Dr Coleman*) Thank you for listening to us.

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HOUSE OF LORDS SESSION 1992-93

MINUTES OF EVIDENCE
TAKEN BEFORE

THE SELECT COMMITTEE ON SCIENCE AND TECHNOLOGY

(SUB-COMMITTEE II REGULATION OF THE UK BIOTECHNOLOGY INDUSTRY AND GLOBAL COMPETITIVENESS)

Thursday 13 May 1993

BRITISH SOCIETY OF PLANT BREEDERS LTD
Dr I Cubitt and Dr S Hughes

FOOD AND DRINK FEDERATION
Professor R C Righelato, Professor B Jarvis and Mr M A Hunt

CONFEDERATION OF BRITISH INDUSTRY
Dr G Schofield and Dr S Shohet

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THURSDAY 13 MAY 1993

Present:

Flowers, L.	Platt of Writtle, B.
Gregson, L.	Renwick, L.
Hilton of Eggardon, B.	Soulsby of Swaffham Prior, L.
Howie of Troon, L. (Chairman)	Whaddon, L.
Perry of Walton, L.	

Memorandum by the British Society of Plant Breeders Ltd is printed separately

Examination of witnesses

Dr I Cubitt, Nickerson BIOCEM Ltd, and Dr S Hughes, Unilever, British Society of Plant Breeders Ltd, called in and examined.

Chairman

577. Good morning and thank you very much for coming. Would you begin by identifying yourselves. If you want to make a brief opening statement about your position, please do so.

(*Dr Cubitt*) Thank you. My name is Ian Cubitt and I am here representing the British Society of Plant Breeders. I am Chairman of their Biotechnology Working Party, of which Dr Hughes is also a member. My own interest in plant breeding and the BSPB is as a member of a seed company, which is Nickerson BIOCEM Ltd, whose shareholders are a French company, Limagrain, and we are the third largest plant breeding company in the world. The plant breeding industry has been involved in biotechnology in the last few years because it sees biotechnology as a more efficient and more effective way to breed plants. The British Society of Plant Breeders represents the majority of United Kingdom plant breeders and is concerned with the legal and regulatory issues related to the application of biotechnology to plants. There are two ways in which our industry will use biotechnology. It will use it either for diagnostic tests which are not covered by regulatory control or for production of genetically modified organisms which are covered by regulatory control. Our position on regulation is that we are very much in favour of regulation of novel technology but we do think that there needs to be a balance between regulation and practical operation in the industry. I think perhaps that is sufficient as an introduction and I will ask Dr Hughes if he wishes to add anything else.

(*Dr Hughes*) Thank you. I am Steve Hughes and I regard myself as a practitioner of the application of technologies in plant molecular biology to plant cell biology and plant improvement through breeding. A part of this involves the application through the rules on transgenic technologies, that is, it involves new plant varieties as GMOs. Further to what my colleague has said about the British Society of Plant Breeders, I should say that we do contribute to the international and to the European debate on regulation through some of the parent organisations to which we are affiliated, notably COMASSO in Europe and ASSINCEC internationally, and in particular our conversations on regulation within the European Commission have been very much through that route. My own areas of activity are that besides contributing to the production of new plant varieties from our base in plant breeding, namely, Plant Breeding International Cambridge, and other base within the Unilever laboratory at Colworth House. From the point of view of agricultural productivity, I am also involved at the interface between plant breeding and food technology in terms of the quality of the products coming from agriculture. As you probably appreciate, the quality of the products coming from agriculture are to a large extent genetically determined as well as being to some extent environmentally determined, which means the breeder has an opportunity to influence those. When I talk about quality I am meaning things besides eating quality and diet but also factors such as post-harvest deterioration and applicability to processing. So I think that gives you a range of the sort of activities that I am involved in in the areas of regulatory activity which I have to take note of.

578. Thank you very much. Taking plant breeding as a whole, how much of it is done by biotechnology means rather than "naturally"?

(*Dr Hughes*) We run into a problem of definitions of "biotechnology", I am afraid, at this point. I have to use the broadest context to give an answer to this question but there are a lot of them. That is why I used the terms "plant molecular biology" and "plant cell biology" in my introduction because there are a number of applications of plant molecular biology which could fall within the definition of biotechnology which do not involve genetically manipulated intervention in the germ line of the plant, and these are becoming of increasing significance to the breeding industry. We call it "molecular marker technology" which enables us, through conventional plant breeding, to have much increased precision and much increased efficiency and reliability. So at that level we see a great impact in this country, and all the plant breeding organisations and companies, even down to small plant breeders, are starting to use these levels of technology. The interesting thing is that they employ all the techniques and all the technologies required for genetic engineering but not to the extent of direct intervention into the plant varieties that they produce. At the level of GMOs, that is, new plant varieties that contain information that has been brought in from other species and other plant families, we can expect a contribution to plant breeding in the longer term. Experiments on the construction of plants of that sort have begun, but

[Chairman *contd.*]

one thing you will appreciate is that breeding in terms of product development has a very long lead time, of the order of ten or, for the worst, or most difficult crops, 20 years, to produce a variety from the start point. So I think you can appreciate that in terms of timing, where that becomes important in terms of positive cash flow, the generation of actual benefits in the market place will take some time.

Lord Flowers

579. Could a few financial figures be put in to illustrate what you are talking about in financial terms?

(*Dr Cubitt*) It is very difficult to give figures at the moment.

580. Order of magnitude then?

(*Dr Cubitt*) Order of magnitude, I would say we do not know. We can perhaps estimate the level of investment that is being made in biotechnology in the plant breeding industry but there are no products derived from genetically modified organisms on the market. It is very difficult to give market projections because really what we anticipate is that in due course of time all the products we sell will have included at some stage in their development either marker technology or have a parent somewhere down the line which was a genetically modified organism.

581. What is the order of magnitude of the expenditure by the industry over the ten-year average development period?

(*Dr Hughes*) I can give you some round figures. The cost of developing a wheat variety, by conventional breeding for instance, is of the order of £1 million. That is actually to take it from the start point to having launched it on the marketplace.

582. That is chicken-feed, really?

(*Dr Hughes*) Yes, but may I make one more point to your Lordships. The overall revenues of the breeding industry may appear quite small as are the costs and the turnover, but the impact of the improvements we bring about in terms of their agricultural payback are actually quite large. So one per cent on overall agricultural productivity is a big number.

(*Dr Cubitt*) Also, I think if one compares use of biotechnology in plant breeding with applications for medical developments, we suffer from the fact that we are a relatively poor industry and yet we are likely to have a significant effect on food production and the environment, both in the United Kingdom and internationally, so this industry is under great strain in terms of funding and adopting novel technology when it is struggling to keep its head above water at the moment.

Chairman

583. Turning to the regulations, in your written answer to question 6, you are very definite that you do not like horizontal regulation as it currently operates. Can you see the Directives moving away from horizontal and, if you do, in what direction?

(*Dr Hughes*) We would very much like to see them move away from the current horizontal strategies and our hope and expectation would be that they would be superseded by vertical regulations, product sector by product sector. Our reason for saying that is that we need to work with these regulations alongside existing regulations, vertical regulations for our sector in the seed business and in plant breeding. In placing our varieties on the market we have to go through a sequence of regulatory strictures that are imposed upon us or we work through the MAFF. These are quite complicated. They take several years to happen and I think it is very important that other regulations that we have to work to should run in a similar vertical direction and I think that really is what underpins our wish and requirement for vertical regulation to cover our sector. I think the other reason is that vertical regulation in terms of genuine risk assessment, the ability to fix on those things in which we should take an interest, as opposed to putting things into categories, is much easier to work in a vertical than in a horizontal sense. So we would very much favour the construction of decision trees, for instance, which work in a vertical direction, to determine what sort of evaluation we have to place on our products before they go onto the market.

(*Dr Cubitt*) It is perhaps worth mentioning that we felt the start to regulation in this area, which was very horizontal, coming from European Directives was very bad because we found plants were placed in the same category as micro-organisms and there was very very little understanding of what a crop in a field was like which was going to be the ultimate product. However, we have moved a long way in the last two or three years and there is now a much greater understanding, both within the United Kingdom departments and in the EEC, that plants in fields are our product and not micro-organisms in a fermenter. They really have taken more and more into account—we have gone through the stages of discussion—that the regulations and safety aspects of these two types of product are quite different.

584. Do you see any area in which horizontal regulation might be appropriate?

(*Dr Cubitt*) I think we could see that integration of regulations on genetically modified organisms and genetically modified plants with seeds regulations would work perfectly well, although one must add that the ultimate product is food. Steve comes from the food industry, so perhaps he would like to comment on that level of integration. But, no, I think vertical regulation could control the development and release of a product onto the market and into the food chain.

(*Dr Hughes*) If I could add a point to that, I think horizontal regulation has a role to play in the early phases of the new technology before it can be pinned to specific product areas, but once the technology itself has been around long enough to be evaluated, which in this case we have been working with genetically manipulated organisms for over 20 years now, within a closely supervised system, I think that that period is over for that form of activity and now we should look at the actual applications and do a vertical risk assessment of what is needed in the regulatory sense.

585. That is very clear. You know precisely where you stand on that. We were told by the Department

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of Trade and Industry that "firms should not be faced with unnecessary duplication of testing and authorization procedures" and that procedures ought to be streamlined "so that one assessment and notification procedure covers all that is required for product authorization". I imagine you agree with that?

(*Dr Cubitt*) We do, yes.

586. Could you give me an idea of how you think the Government should go about setting up such a revised regime?

(*Dr Cubitt*) One thing that we find very useful in considering this are decision trees where one looks at it aspect by aspect because, as was mentioned earlier, the first question is, are you dealing with a product that should come under the regulations at all and, if it comes under the regulations, what part of the regulations? If that risk is considered acceptable under one part of the regulations, for example, at the experimental level, then what about at the marketing level, and so on? We find decision trees are a very easy way to follow through the development of a product and the regulation of a product right through to marketing. We feel that those would allow integration of the different types of regulations which are around at the moment. As regards streamlining of procedures, yes, we are encouraged that the United Kingdom is in favour of streamlining procedures and, in fact, in practice, when we are dealing with field trials and permission for field trials for genetically modified plants in the United Kingdom, streamlining of procedures and allowing the industry to carry out the same tests perhaps in fields for more than one year is already beginning to happen and we are pleased to see that progress.

587. I understand that some of the Directives might be revised in the reasonably near future, discussions are going on. To what extent is your society involved in these consultations, presumably with the Department of Agriculture?

(*Dr Hughes*) There are a number of routes through which we can contribute. The one I already drew attention to is through the European Association of Plant Breeders, through COMASSO, and the other by consultation with our own ministries. There are a number of current Directives, ones established like 90/220 which will have to go through revision but, also, ones coming through the system, which can learn from them such as the Novel Foods Regulation coming out of DG III, currently being discussed in the European Parliament, and then the Seeds Directive, which is especially close to our sphere of operation, coming out of DG VI (Agriculture). We are particularly interested in both of those, contributing as much as we can to the discussion, especially since the Seeds Directive embodies the whole of the Novel Foods Regulation as it is currently drafted. We would look forward to consultation with the Ministry of Agriculture on that particular Directive. So far, our discussions and examination of the draft forms of that Directive have been through our parent organisations.

588. Have you found your discussions with the Ministry fruitful in the past?

(*Dr Hughes*) Yes, especially with respect to 90/220 where the Department of the Environment had a very big job to do in terms of adapting a Directive specifically to work with plant breeding, which is something they had not had to think about previously. We actually played a fairly big part in educating them and making sure that there was a pragmatic level of interpretation of that Directive which would enable us to actually work at all with it. I think we have played a part in that consultative process, but we would always wish to do more.

589. Since you are involved in agriculture, food and so on, food is an area where the public show a certain amount of concern. How do you stand on labelling of foods to indicate some genetic origin?

(*Dr Hughes*) This is something I have been involved with and talked about for some time. We were asked to comment on the earliest draft of a labelling proposal from the Foods Advisory Committee of MAFF, which at that stage we thought was not a useful contribution to the debate. They have recently come out with a second consultative paper which I think sets the basis for a very good developmental debate of an approach to bringing information about food products to the consumer, to the level at which it is relevant to their decision-making process. My feelings about it are yes, we need to inform consumers about things that are significant to their decision-making process. What we do not need to do is unnecessarily alarm or confuse by adding blanket labels about technological processes. So we would not be expecting to see a form of labelling ultimately that attempted to categorise products on the basis of the technologies used to produce them, more a form of information that enabled the consumer to know what the composition was and, where necessary, the genetic provenance of the materials going into food products, where their mixtures came from.

590. Let us put this at its simplest so that I can understand it. You would like to see a system where a customer would go into the baker, he would see a loaf which had a label stuck on it which said: "This loaf was at one time wheat which had been genetically manipulated." You would not like to see that, would you, or would you?

(*Dr Hughes*) No, because I do not think that is relevant to his decision-making process. Once a wheat can be approved as being wheat it should be able to move through the food chain freely without anybody needing to think about that factor further, but if the wheat had something novel in it from an organism which potentially could have an allergic response in a certain percentage of the population such that some people needed to avoid food with that component, then I would say one would expect to see that demonstrated through a label. So I think that principle as developed by the Foods Advisory Committee is sound but is still a very difficult one to come completely to terms with and it will need a great deal more debate and probably its own decision tree to develop a workable and pragmatic system.

(*Dr Cubitt*) I think one should perhaps consider this question of labelling in view of the fact that many of the things we will do to plants will not affect the

[Chairman *contd.*]

final product. Many of the genes we are dealing with may be expressed and produce proteins, for example, for insect resistance in a leaf without affecting the product quality of the grain at all. So we would prefer regulation which is based on the quality and composition of the product rather than necessarily something which is of much less relevance to the consumer.

Lord Flowers

591. Could I press you a bit more. You are, of course, absolutely correct in my view in what you are saying, but the public perception is that when you genetically manipulate something you change it in some way which has dangers about it. So we are not really talking about wheat, we are talking about genetically engineered wheat. Should you bow to public perception, however incorrect scientifically, in such things as food labelling, on the grounds that you have to get people used to dealing with these things and it may be the best way of doing it rather than giving the appearance that you are hiding something?

(*Dr Cubitt*) The position we are in at the moment is that the technology works and works increasingly well and is becoming increasingly specific and sophisticated. So the big problem, if you like, that we have, is public perception of what we do and whether the products that we sell will be acceptable in the United Kingdom. It is quite clear that there are parts of the world which are short of food where these products are likely to be readily acceptable and they will impose their own regulatory controls. As we are aware, the United States is ahead of Europe in terms of development of products, and once you have a product that is produced, say, in the United States and is imported into Europe, it is impossible to analyse that product *per se* to decide whether any of the plants or any of the parents used in the development of those crops was at one time genetically modified. So there are certain practical difficulties. When one comes to the public perception area, we have to be careful that the information we supply is meaningful and does not stop products getting to the market because people develop a perception which is not actually based upon a meaningful analysis. This is a complex area and the British Society of Plant Breeders is seeking advice at the moment on how we should go about addressing this area because, of course, we have been modifying plants by many methods for many years and for us in some ways this is just another technology which will help our production of new varieties. I am sorry there is no easy answer, in fact we would appreciate any advice, as to how we might tackle this problem of public perception of a technology, especially when we are dealing with plants, because very often we may get tarred with the same brush as somebody working with animal work where there are ethical or other considerations which may not apply to plants. We are sensitive to the fact that the whole industry has to behave responsibly or somebody could do something which gives us a bad name and damages the development of the technology against the nation's interests as well as our own commercial interests.

Baroness Platt of Writtle

592. Do you go into schools with what I call objective information?

(*Dr Cubitt*) We do to some extent. Our own company has been involved in training people who work in the Science and Plants for Schools programme and helping them to develop experiments which will be used in schools and to educate children about the technology. I was very encouraged last week. I have a daughter of 17 who is being taught in school already about the work which Ciba-Geigy have done in the United States in the development of insect-resistant corn, and the way she has been taught that in school I was very pleased about because she came forward with very positive views that this was a worth-while development which would reduce the use of insecticides in agriculture. So the answer to your question is yes, we are involved. Of course, one can never do too much.

593. No. I think there are amongst the teachers great uncertainties and, therefore, they will need to have their own fears helped before they can teach it in a way which is objective and positive to children.

(*Dr Cubitt*) Yes.

594. The only way really is for people who are involved and working in the industry to be providing interesting and inspiring literature. I am an engineer and the Engineering Council is doing the same sort of thing with Neighbourhood Engineers and perhaps that idea could attract people who are involved in your industry into schools to talk about their work.

(*Dr Cubitt*) I am very encouraged by the work which the SAPS programme is doing, which is well organised and effective.

Lord Soulsby of Swaffham Prior

595. You mentioned the end product and you took wheat as an example. I would agree with what you said but there is also the question of the farming practices that lead to the end product. You mentioned that you have been in the field of plant breeding for many years and often that has meant increases in nitrogen and a whole variety of new farming practices. Do you take these into consideration with new breeds with genetic modification or biotechnological approaches?

(*Dr Hughes*) Yes, breeding for reduced inputs with that as a positive target for reduced input of chemicals, reduced input for fertilisers and control agents, is always one of our objectives, as is breeding for improved resistance against damaging organisms and predators of the crop. That is in the broad sense sustainability, always thinking at the time of breeding how is this going to contribute to sustainability in the long-term because, of course, that is our future as plant breeders, to supply improved varieties for the developing world.

596. So you would claim that your new varieties are geared for the environment too in that your inputs are going to be reduced?

(*Dr Hughes*) That is our intention, yes.

(*Dr Cubitt*) I think, as you are well aware, you can address almost any problem that one can think of in

[Lord Soulsby of Swaffham Prior *contd.*]

terms of growth of plants that is based ultimately upon genetics of the plants with this technology. So if you want drought resistance plants or you want plants with different proteins or insect resistance or more efficient use of nitrogen, all this is possible if we address ourselves to specific problems. Obviously we do one or two at a time.

Chairman

597. Could I go back to a point earlier about the financial aspect. You were quoting £1 million for the development of the new breed of wheat and that is quite minimal compared with new vaccines from animal products. What is the patent situation with new plants? Can you patent these and claim intellectual property rights over them or are they free to be used by anyone, once you get them into the market production?

(*Dr Hughes*) There are two routes and avenues to the protection of the intellectual property present in a plant variety. I should say, expected to be two routes. At the moment, we have a system of plant variety protection which is based on an international convention which enables the breeder to recover royalties on those who multiply and sell the seeds. Each variety is protected as a single entity, so each new variety of wheat, for instance, has a name and is recognised as such as being something novel and different. There are certain obligations placed on the plant breeder in return for that right which are that he makes his material available to others to breed the next generation of crops from, for instance. With the advent of genetic material coming in from novel sources into plants but using slightly different technological approaches, then we have the possibility of the imposition of conventional patent protection. I say conventional because it needs to be altered in some of its principles to take account of the differences in plants. Both these routes of the protection of the intellectual property in plants are currently under debate within the Commission. There is a Directive and a regulation currently under debate. They are very complex issues, especially when you have both systems operating side by side in association with a single variety, but we see these as both essential to in fact protect the investment that has gone into the process of developing those plants. I should make another point there, although it is £1 million to develop a wheat variety and this is spent over, say, 15 years, the product life cycle is short, so, in fact, you have to take account that we have 15 plant breeding programmes for a wheat variety growing in parallel, each one a year staggered behind the other. The investment in breeding of a new wheat variety at any one moment is all those programmes added together. So, in fact, the cumulative investment is quite large, especially in association with the size of most plant breeders.

(*Dr Cubitt*) The plant breeding industry is actually a relatively small industry and it has relatively low profitability which is why we think £1 million is quite a significant development cost, whereas we appreciate for a pharmaceutical company it is peanuts.

Chairman

598. I notice from your paper that you object to farmers having the right to save seeds without paying any royalty. There are a lot of farmers and they are very cunning people. How would you prevent them doing that?

(*Dr Hughes*) At the moment we have a system which allows the farmer to produce his own seeds for his own use once having bought a variety.[1] In general it is not in his interest to do this too often because of the quality constraints and the superior quality of the seed that can be provided by the seed multiplication industry itself, but it does appear in most countries as a privilege that the farmer assumes. A suggestion is that he should be asked to pay some sort of reduced royalty on the basis of doing that. Policing that is, as you say, a rather difficult prospect and it is a problem that the seed industry does not deal in what we call F1 hybrids which cannot be multiplied by the farmer for his next generation. It is a problem which the seed industry may have to live with.

599. To get used to?

(*Dr Hughes*) Yes.

(*Dr Cubitt*) I think the fact that we have had plant variety rights for some period in Europe is very important because it has meant that in European we have had a lot of breeding of crops like wheat which are self-pollinated and the farmer can easily multiply his own seed, whereas, in the United States of America by comparison, the investment in wheat breeding has not been in the private industry, it has been very much within universities and I would suggest that we have made much more progress in Europe because we have had a much more vital wheat breeding industry than in countries like the United States of America where they have had, of course, a much larger area of wheat production.

Chairman: I think we are running out of time. I wonder if my colleagues have any further questions to put?

Baroness Hilton of Eggardon

600. Could I just clarify the intellectual property rights distinction. It seems to me that one of them is horizontal and one of them is vertical, in terms of what we have begun to understand about the differences between those terms, that one relates to the process by which you produce these and the other one relates to the final product. Is that a reasonable analogy?

(*Dr Hughes*) No, I do not think strictly it is a reasonable analogy because what is— I assume you are thinking in terms of that as being the process-related route to protection?

601. Yes.

(*Dr Hughes*) What is patented is an application of a particular bit of genetic machinery, for instance, not the technique of putting it there.

602. It is not a new scientific method that you are patenting?

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[1] Note by the witness: Though this is by default rather than by the intention of plant variety rights regulation.

[Baroness Hilton of Eggardon *contd.*]

(*Dr Hughes*) Right. There are attempts to patent some aspects of the process of putting genes into plants. That does have a horizontal component, it is true, but those would be a minority of the actual working patent library that we actually function with ultimately and one can also expect that because of our long lead times a lot of those patents are fairly old by the time the rear revenue streams are operating.

Baroness Hilton of Eggardon: I thought I would find a simple way of understanding that!

Lord Whaddon

603. We have heard from other interested parties in genetic manipulation that they fear industries will be squeezed out of Europe because of the rather hostile environment for regulations in Europe. Do you see any such dangers in plant breeding, that work maybe squeezed out of Europe?

(*Dr Cubitt*) I do not think the plant breeding industry will be squeezed out. The most that could happen is that we would be squeezed to using old technology. One of the things about plant varieties is you have to develop them locally because they are adapted to the local climate. So you cannot take a wheat variety from the United States of America and grow it in Europe without doing some development work in Europe. You need local development work even if sophisticated technology was done elsewhere.

Chairman

604. I think we will draw to a close now. Thank you very much indeed. Should you wish to draw any further matters to our attention later on we would be very pleased to hear from you.

(*Dr Cubitt*) Thank you.

Memorandum by the Food and Drink Federation is printed separtely

Examination of witnesses

PROFESSOR R C RIGHELATO, Ashbourne Biosciences and Chairman, Food and Drink Federation Research Working Group, PROFESSOR B JARVIS , Technical Director, HP Bulmer Ltd, and Member, Food and Drink Federation Research Working Group, and MR M A HUNT, Secretariat, Scientific and Technical Division, Food and Drink Federation, called in and examined.

Chairman

605. Thank you very much for coming. Could you identify yourselves for the record, and if you care to make a short statement about your position, we would like to hear it.

(*Mr Hunt*) Thank you, my Lord Chairman. Might I say by way of initial introduction that the Food and Drink Federation, which we are representing this morning, is the leading major voice for United Kingdom food and drink manufacturers and we in turn have membership of an equivalent body at the EEC level, so that we are discussing biotechnological matters with EEC Member States' industries and with the Commission. To introduce ourselves, I am Michael Hunt from the Scientific and Technical Division of the Secretariat of the Food and Drink Federation, or FDF for short. My expert colleagues from the industry are, on my left, Professor Renton Righelato, who is Chairman of our Research Working Group at FDF and our principal spokesman this morning, and is from Ashbourne Biosciences, and on his left is Professor Basil Jarvis from HP Bulmer Ltd. Perhaps I might ask Professor Righelato to make a few introductory remarks on our memorandum before we move to questioning.

(*Professor Righelato*) Biotechnology in its broader sense, of course, has been the basis for much of the technology of the food industry for a long time. As biological knowledge has developed in lots of spheres it is naturally assimilated into use in the food chain. I suppose we essentially see molecular genetics in that same light. It is an extension of existing knowledge which will become quite pervasive in its application to the food chain, as pervasive as, say, Mendelian genetics was through the last century. We do not see that molecular genetics *per se* presents any new issues for food safety and we believe that the existing regulatory framework for foods can handle the sorts of novelties which will arise as a result of the application of molecular genetics to our raw materials. So our concern is primarily with the development of a sensible regulatory structure for novel foods at a European level. We have been involved with the European Commission in the development of the proposed Novel Foods Regulation and are in discussions with both the Commission and MAFF in this country. Of course, we are aware of public unease at new technology in general in the food sector and in molecular genetics in particular. We are aware of that unease. We believe that it should be addressed primarily through information and education; and that it is not really something which we can effectively address through legislative procedures. The details of our comments are in our memorandum.

606. Thank you very much. I am sure you are right when you talk about the education process. I do remember the long campaign in favour of proper beer instead of that material you got in a keg and that was done by means of argument and persuasion and so on rather than by regulation. I have a feeling that lies behind your general attitude here. Let me say something about this question of horizontal and vertical regulation. I may have misunderstood your paper but you seemed to me to be rather in favour of product-based regulation but at the same time you say that environmental legislation must be horizontal. How do you propose to combine the two?

(*Professor Righelato*) There are two issues with which we are concerned. One is the assessment and control of environmental risk, which should be independent of the use to which the product is put. It is a function of the environmental exposure, and whether a plant is used for making a chemical or whether it is used for making a food, it should be subject to the same environmental assessment. I fully

[Chairman *contd.*]

take the point that was made by your previous witnesses that there are some substantial differences between pharmaceutical issues or those sorts of genetic manipulations carried out for pharmaceutical end products and those carried out for agricultural end products, and I can fully see the difficulty of combining those two in a single regulation. That was one of our problems when we were, at a very late stage, called into the consultation on implementation of the Environmental Deliberate Release and Containment Directives. The two, for example, pharmaceuticals and foods, do not sit easily together. But I would stress that within food we see a need for a single, what across industries we would call a vertical, regulation for food safety issues.

Lord Perry of Walton

607. It is a silly question in a way but at the end of the food chain you are selling materials rather than plants. I know that DNA is destroyed if it goes through the mouth or the digestive processes but what is the stability of the DNA in respect of cooking and heating and all the rest of it? Does it survive at all?

(*Professor Righelato*) DNA is a very stable molecule. These are really questions which should be asked of the Advisory Committee on Novel Foods and Process. The great majority of DNA is broken down before it gets into the body. It is broken down in the gut, if not before, and, of course, in many food processes the DNA from the plant never ends up in the food product anyway. If one is making a vegetable oil or sugar those parts of the plant which contain the DNA have been removed.

(*Professor Jarvis*) The exception, of course, is where the product which is being consumed is a direct fermentation product which actually contains viable organisms. Yoghurt is an example where clearly if there were to be an organism used which had been manipulated in an appropriate manner, the DNA would actually be consumed in its native state. But as you rightly say, the DNA is then broken down within the body, in the gut, in the same way as many other organisms.

608. If I can press you a little further, if you have a new variety of wheat which is genetically modified, is the DNA in the flour? Is the DNA in the bread? At which stage does it disappear?

(*Professor Righelato*) In that particular case the DNA carries through to the final product. It is ingested and broken down in the gut.

Chairman

609. There is something you say here under question 3. You say that "molecular genetic techniques provide faster, more accurate development of new varieties than conventional breeding" and you then go on to say that they are "less likely to have unintended side effects." How can you be sure of that?

(*Professor Righelato*) In so far as one is transferring a small amount of defined genetic information, one can be more precise about what one does to the plant than in conventional breeding techniques where you are swapping rather large amounts of DNA and the outcome is much more subject to chance.

610. And you think that your transformed food is the same kind of thing as the natural food?

(*Professor Righelato*) For food which has been made through a genetically manipulated organism, there will be some reason why it was manipulated in the first place. That may be reduction in cost of the agricultural product, in which case what comes through into the food chain is the same as the comparatively more expensive, unmanipulated material. If a new character is introduced, such as a better flavour or a different ripening characteristic, that does carry through; the consumer does see that. Does that answer the question?

611. Yes, it does, and that brings me to the labelling point again. Clearly you can genetically manipulate fruit to give it better colour and a longer shelf life and all these things. Would you like such food to be labelled as having been produced or transformed in some genetic way?

(*Mr Hunt*) I think fundamentally and scientifically once any such transformation has been approved for entry into the food system there is no need to label that, but we do recognise, as has been discussed already, the need to consider consumer information and to inform the consumers' decision-making. In that respect, we too welcome the current discussion paper that has been put forward by the Food Advisory Committee. We agree with the Food Advisory Committee that labelling itself cannot substitute for consumer education and so, to answer your point Sir, if such products are labelled, and there is no background of consumer education, it is extremely difficult to so do without putting people off the food altogether. An approach has to be taken whereby criteria are established, agreed criteria by which it can be decided whether or not labelling is necessary. The Food Advisory Committee has most usefully set down such criteria and we also would like to see such criteria developed into some sort of decision tree so that the industry could much more readily decide whether there were genetic aspects of the finished product which did for any reason require labelling. The Food and Drink Federation at the moment is considering those criteria and we would like to see as an outcome some decision tree process, some means whereby the decision could be made, some suitable forms of words which could be used for the labelling of a very clearly specified and limited number of cases where it was considered necessary. That is, at the present time, the enormous problem, that the words we use are absolutely vital and virtually impossible to arrive at. It is an extremely difficult position which leads only I think to the conclusion that the essential background is adequate consumer education so that a judicious use of labelling, where considered necessary, does actually mean something. It is vitally important.

612. I think you are just being diplomatic. I think your view really is that genetically manipulated foods are much the same as any other and that special labelling would be inappropriate. Am I right or am I overstating the case?

[Chairman *contd.*]

(*Professor Righelato*) I think broadly our view is that genetic manipulation *per se* is not an issue for labelling, but that there may be things which have been done to the food which do make it sensible to inform the public about it, for example that it contains or does not contain certain allergens, that it contains the product of a gene of an animal which some particular groups may find objectionable, which are very specific bits of information which a consumer can make use of.

Lord Flowers: My Lord Chairman, if the public is worried about marginally ill-effects of genetically manipulated products, it is up to a manufacturer to say, "This product contains no genetically manipulated material." In that case you are almost bound to follow it by saying something if you are a producer of genetically manipulated material. What are you going to say?

Chairman

613. While you are thinking about it, could I expand that question just a little? I am thinking of the fact that you can go into a shop and buy what is described as organically produced bread rather than whatever the other kind is. Would you want to see some very simple labelling? Do not forget the first question.

(*Professor Jarvis*) I think in the first instance, as has already been intimated, we would certainly not wish to see a generic statement such as "Contains products of gene technology" or anything of that sort. Clearly, if we were to take the negative labelling approach, such as you have suggested, where it would be analogous to the situation where people say, "No preservatives", or "No artificial colour", as I am sure you are aware, Sir, that approach has been frowned on by the Food Advisory Committee and other bodies as being not a desirable form of labelling, other than as general consumer information. I see a continuum within the food product chain from those products which are essentially no different whatsoever, albeit they have come from genetically manipulated ingredients or genetically manipulated agricultural products, all the way through to the situation where there will be the use of perhaps genetically modified micro-organisms or a fermentation process which may or may not actually affect the food itself in the sense of improving quality and so on, all the way to the far extreme of the potential of the use of transgenic animals. Clearly we can visualise various implications of food safety, we can visualise different implications of the ethical and religious taboos throughout that continuum. By using a decision-tree approach, I think it can be realistically argued that if the basic product is no different from the normal, then there is really no need or justification for any labelling over and above what is currently required but, as you go more to the extreme end, then I believe almost certainly there will be requirements to actually make it known in general to the consumer that such a product has been produced by modern techniques.

614. Would I be wrong in saying that the public have the right to command things however silly? That manufacturers have the right to put things on labels if they wish saying that this does not contain something or other, and the problem really is one of educating the public not to be fearsome of things that they need not be fearsome about.

(*Professor Righelato*) I think that is exactly the point that we would support. That it is very much a matter of educating, as the Food Advisory Committee says.

615. What are you doing about educating the public?

(*Professor Jarvis*) The Institute of Food Science and Technology has, in fact, set up a group to prepare information for consumers on food biotechnology. In addition, the Food and Drink Federation has developed in recent times a schools' education programme on food safety, food technology and nutrition and that could possibly be expanded into the specific areas of food biotechnology. As I think was suggested earlier this morning, it is undoubtedly the case that it is the teachers who in the first instance need to be educated because they can give many misconceptions to their pupils if they actually fail to understand the basics themselves. There is also, in the wider context of biotechnology a number of biotechnology, education programmes specifically orientated at schools; for instance, the University of Reading has a schools' biotechnology programme which is geared to introduce school children to the whole concept and range of subject areas within biotechnology. There is the start of a lot of educational activity but, in general, I am not sure if the consumer would prefer to have assurances from Government or whether the consumers are sometimes as cynical of assurances from Government as they are of assurances from industry or the scientific community because, of course, we have to recognise that science in this country does not hold a particularly strong position. Therefore, I think we do need to have a concerted educational approach which involves the use of inputs from industry, inputs from Government and inputs from the scientific and technical bodies which will be aimed at educating, not trying to reassure, the consumer as to the real benefits which they will obtain, and that "UK Ltd" will obtain, through the use of biotechnology in the food industry.

Lord Perry of Walton

616. I would very much agree with what you say but educating the public awareness of the principles is a very expensive business. It is certainly beyond the resources of the academic community. It is probably not going to be funded by Government. Is it going to be funded by industry and would it not be a good thing if the various industries that are involved, not just the food industry, were to get together to do this rather than to leave it to the individual industry to do its own little thing?

(*Professor Jarvis*) There were suggestions, Sir, I think it was about two years' ago, that there should be a coordinated Department of Trade and Industry programme concerned with information on biotechnology which for various reasons did not get off the ground.

Lord Flowers

617. I do not want to be a wet blanket but in the United States where the public are better scientifically educated than they are here there is more silliness about these things than there is here.

(*Professor Jarvis*) There is also much more consumerism (if I might use that word) and I think one of the areas that we really need to try to do something about is the media attention and media attitudes to subjects such as biotechnology and food safety, because undoubtedly a considerable amount of harm can be done in five minutes of poor television which can totally wreck many months or years of very positive work.

Chairman

618. I am glad you mentioned that because earlier on you spoke of teaching the teachers. To what extent do you attempt to influence the originators of media activity, whether television or newspapers? I am not just talking here about science correspondents.

(*Professor Righelato*) The Food and Drink Federation does that specifically through its External Relations Divisions and they are right now developing their position on the subject of genetically modified organisms in the food supply. It is something which I confess as an industry we have been rather slow to get under way, but the other side of the coin is that the best way of convincing is in actually seeing some products and being able to eat some products, taste some products and see the benefits, and until they are on the market we cannot do that.

(*Professor Jarvis*) It is essential that we do not repeat the bad stituation which occurred in relation to the whole food irradiation programme over the last 20 to 30 years, otherwise food biotechnology will not continue.

Lord Soulsby of Swaffham Prior

619. My Lord Chairman, might I ask where the Food and Drink Federation stands in its input with respect to food and food processing? Do you help define research needs in the food and drink industry and customer requirements or do you handle those once they have been done?

(*Professor Righelato*) The Federation works very hard with Government to develop research programmes, to evolve the research stratagem, and many of its members provide people who work in the institutes, in the universities, to help out the management of research programmes. So yes, we start very much at the research end.

620. What are the pressing research needs for your industry at present? Could you give me an example?

(*Professor Righelato*) In the context that we are talking of today perhaps the most pressing needs are in the understanding of what it is that controls quality in food products. As an industry we are primarily concerned with uprating quality. Our suppliers worry about getting the cost of their raw materials down. So the physics, chemistry and biology underlying the quality of plant products and animal products is the key to underpinning science which determines what we do and determines what the breeder can do. If he knows what genes he has to manipulate, he can achieve quality improvements much more readily. So that, I think, is probably the basic science area on which we would put most stress.

621. One of the witnesses that we had a few weeks ago complained rather bitterly that much of this biotechnology was to the benefit of the Western world and not very much was being done for the developing world. I would not agree with that but how would you respond to such criticism?

(*Professor Jarvis*) I would agree with you. I do not think it is actually correct. I think a lot of the developments which will come, whilst in the first instance they may be to the benefit of the Western world, will certainly in the long term be very much to the benefit of developing or third world countries. We can see a number of issues relating to food safety which are critically important in developing countries but which have, in many instances, been eradicated over time within the Western world, although, of course, we have our own food safety issues going on constantly, particularly from a microbiological point of view. I think biotechnology will have a very major effect in terms of the economies of third world countries. We would, of course, have to be very careful if significant constraints were placed on biotechnology development within, say, Western Europe and a considerable biotechnology development occured within the food industry in developing countries, not then to introduce artificial boundaries which would not permit the development of their economies based upon the fact that they were using biotechnology procedures which perhaps we would not be allowed to use. So there are a number of ethical issues which have to be considered in this context just as much as in the general context of food biotechnology.

622. The critical point of criticism was that whereas, as you say, much of the development here might filter down into the developing world, there was not much being done which was specific to deal with problems in, say, the Sahelian area or other parts of the world, for example crops grown in arid areas.

(*Professor Jarvis*) Drought resistance work, the possibilities of growing crops at exceptionally high or, in some cases, exceptionally low temperatures by the transfer of appropriate genetic material to enable the crops to grow in difficult conditions will, of course, be very important and undoubtedly will spin off from the technology, and there is work already going on in some of these areas.

623. That is already being done?

(*Professor Jarvis*) I believe so, yes.

Chairman

624. Various concepts we have come across call it the fourth hurdle. I have forgotten for the minute what the other three are but the fourth one was the commodity needed. How do you react to the question, do we really need a redder apple? That is very simply put.

(*Professor Righelato*) Give the consumer the opportunity to make the decision is the approach we take. People obviously do like better quality products because they buy them and it is our objective to provide them with ever-increasing quality products,

[Chairman *contd.*]

and this is one way in which we can achieve that in a number of situations.

Baroness Platt of Writtle

625. So you would have a shelf of irradiated food, would you? As it is for organic at the moment, you would have a shelf saying, "This has been irradiated"?

(*Professor Righelato*) No, that is not the way these products would be likely to be presented. It would be a strawberry which has a fuller flavour and you could take it home and still eat it in three days' time because it has not gone mouldy, and it would be advertised as a better quality strawberry.

626. But not an irradiated one?

(*Professor Righelato*) If one were to be using irradiation then one may require that to be labelled but that is a separate issue.

627. But that is going to be part of the way that the public decides whether they are going to buy or not, is it not?

(*Professor Righelato*) I think the public buy largely on the quality of what they see and taste. In practice, very few people read the label.

628. I am not sure about that.

(*Professor Jarvis*) In general, my Lord Chairman, I think it is true to say that consumers eat and drink using their eyes first.

Chairman: I must say the label that attracts me is the label that says, "Reduced"! We are coming to the end of our time. Are there any further questions from the Committee? Thank you very much for coming. If you wish to add to anything which you have said, please do so.

Memorandum by the Confederation of British Industry is printed separately

Examination of witnesses

DR G SCHOFIELD, Deputy Chairman, CBI Biotechnology Working Party, and Project Leader, Expert Systems in Microbiology Department, Unilever Research, and DR S SHOHET, Secretary, CBI Biotechnology Working Party, called in and examined.

Chairman

629. Good morning. I wonder if for the record you could tell us who you are and where you stand?

(*Dr Schofield*) My name is Geraldine Schofield. I am Deputy Chairman of the CBI Biotechnology Working Party. My own background in industry has been working for seven years with Unilever Research. Before that I was involved in the public health service and in academia. I am a CBI Representative to the Advisory Committee on Genetic Modification and the Advisory Committee on Releases to the Environment. Could I introduce my colleague, who is a full-time member of the CBI and who might like to say a few words of background about the CBI.

(*Dr Shohet*) If I could make a few additional remarks, my Lord Chairman, your Lordships probably already know the CBI. We are fundamentally concerned with the international competitiveness of British industry. Members of the CBI come from manufacturing, finance, employers' organisations and trade associations, including chambers of commerce and to a certain extent, the public sector as well. In fact, more than 250,000 public and private companies are therefore represented. In terms of biotechnology, the CBI's interest goes back a number of years to the late 1970s. To give you a potted history, the CBI was asked to submit evidence to the House of Commons' Select Committee on Science and Technology, their Genetic Engineering Sub-Committee, back in the late 1970s. It was also asked around about the same time to give evidence to the Genetic Manipulation Advisory Group of the Health and Safety Executive on risk assessment issues. As a result of these activities, it was realised that a specialist group of industry experts was needed within the CBI and a genetic engineering working party was formed in 1979. That was very much an *ad hoc* group, meeting on an informal basis, really sort of exchanging views between companies and trade associations with the trade associations very much leading on sector-specific issues. In 1988, it was decided to reactivate the CBI's role and to widen its membership, partly in response to the Commission's draft Directives 219 and 220. Subsequently, the CBI formed a biotechnology working party and this has since held regular meetings discussing the broader issues. Just to give you a brief resume of my own background, I am an agricultural scientist by training. I have a doctorate in plant biochemistry and post-doctorate experience in plant biotechnology. I joined the CBI in 1991 to cover biotechnology issues and I also act as a policy adviser in a number of general technology areas.

Chairman

630. Thank you very much. Can you tell me to what extent the CBI has been involved in the consultations leading to the draft Directives 219 and 220 and are you being consulted now about any future Directives or amendments?

(*Dr Schofield*) As Simon mentioned, some of the United Kingdom companies were alerted to Directives on biotechnology, 219 and 220, and Protection of Workers Directive in around about late 1987. My own company was one of those. I think it was flagged up to us, in fact, by the Laboratory of Government Chemist, from the DTI. At that point it was already quite a firm draft that some of us saw and one of the reasons for the formation of the CBI committee at that point was actually to discuss the very broad issues contained in 219 and 220. There was not really a consultation, as such. We were told by the DTI what was going on, but the DTI themselves were not involved at that point. It was a group of United Kingdom national experts who

[Chairman *contd.*]

were, the Department of the Environment, the Health and Safety Executive and MAFF which led in terms of talking to the Commission. That was how we came into the discussion. As I say, we were given a fairly formal draft which we discussed and it was really very much a matter of making a few representations to United Kingdom Government, but we did not know how far they went in terms of taking it back into the Commission. We were not really informed of any feedback. It was very much a one-way flow of information. In terms of what is happening today, we have been a little more informed through our representation to ACRE (the Advisory Committee on Releases to the Environment) and we have had much more of a communication flow since then, including talks with the Department of the Environment. Communications with the Health and Safety Commission have always been extremely good via the CBI. One of the things which we are looking at now, is that there is going to be a reformation of ACRE. The current committee is going to be dissolved next month and we have no idea what will happen then in terms of the communication with the Commission as this was our main source of information in recent times. We hope that it will continue but we are not sure what is going to happen in that respect at the moment.

Baroness Hilton of Eggardon

631. Why is it being dissolved?

(*Dr Schofield*) It has a three year term of office and, under the regulations which came out in February this year, it is now a statutory committee and is being reformulated, at the moment we have no idea what the constitution of the new committee will be.

Chairman

632. Do you find these arrangements satisfactory?

(*Dr Schofield*) Certainly through ACRE, ACGM and the ACDP (Advisory Committee on Dangerous Pathogens) we have had a very good flow of information. We did have a communication problem with the Department of the Environment which was substantially helped by our membership of the Advisory Committee on Releases into the Environment.

633. Still on these Directives, I notice in your answer to question 5 about regulations, in the last sentence you speak about "major problems of scope-setting and definition", which you describe as "the basis of concerns." Would you like to say something about that?

(*Dr Schofield*) Yes, we have already heard something from my other colleagues about the so-called horizontal versus vertical regulation debate. The problems of 219 and 220 are really their attempt to cover a multiplicity of uses of biotechnology in terms of end product. For example, when one was interpreting the Contained Use Directive 219 and its interpretation to the law of the United Kingdom, that was also taken to interpret plants as well as micro-organisms. The original Directive was actually only contained use of micro-organisms, not the contained use of plants or animals. So the interpretation was broadened considerably in the United Kingdom, which caused a lot of problems with the scope of the Directive, because it was never intended to cover those other organisms. In terms of the release Directive 220, once again, you look at Annex 2 of that particular Directive, it is very much an orientation towards release of micro-organisms, not in terms of release of plants and, we have also heard from the BSPB the problems of wider interpretation on very different product sectors. This would also include, I am sure, the health care people, whether there is a need to go through some kind of release Directive in terms of vaccines. It is, once again, trying to interpret a particular rather definite Directive in terms of very different product sectors and this is one of the problems that we did have and, we see are still coming through into the product legislation today.

634. Is this one of the reasons why further down the same page you say that attempting to transport the EC Directives from horizontal to vertical would lead to problems?

(*Dr Schofield*) Yes. I do not think one is looking for any sort of evolution in terms of horizontal to vertical. In terms of the process of biotechnology, which I am sure a lot of people have said to you is a tool, we are looking at health and safety of people and obviously protection of the environment, particularly in the research stages, and this has been happening for some time in the United Kingdom. For example, people working with plant pathogens in the laboratory situation have to work to certain guidelines and we have had to work with health and safety rules for many years. When you are looking at putting products on to the market, it is not just a question of safety, it is also a question of the efficacy of the product, its nature, its usage, and whether it actually does what it says it is going to do. There is a whole raft of other things which come into product legislation. So, as I said, it is not really a transition. One concedes that we need regulations in terms of health and safety. We also need very specialist regulation to cover vaccines, to cover foods, to cover food ingredients, pesticides and so on. There needs to be a whole different set of approaches to each different product.

Baroness Platt of Writtle

635. You are really firmly in favour of its being sectoral in that situation?

(*Dr Schofield*) It has to be, I think, because, as you said, there are going to be specific problems which are peculiar to health care products and vaccines which could not possibly apply to, for example, microbial enzymes which are used for industrial purposes. There are going to be quite different sets of problems in terms of products and having to regulate a product.

636. Do 219 and 220 in any way divide into sectors or not?

(*Dr Schofield*) Not at all.

637. Will they? Is there any possibility that during the consultative period they will divide?

(*Dr Schofield*) In the adaptation to technical progress, which the Commission are undertaking at

[Baroness Platt of Writtle *contd.*]

the moment, there is an attempt to modify some of the annexes and modify some of the scope so that when we have specific product legislation, then you can easily take, for example, part of Directive 220, which is environmental protection, and incorporate it into product legislation. So you do not actually have to go through two or three different sets of regulations to get a product to market, but they do not lend themselves to a product approach.

638. Is it possible that the United Kingdom could translate them into a product approach or is that going against the Directive?

(*Dr Schofield*) It would have really to go through adapting the Directives themselves.

Chairman

639. Is that not what the Belgians would like to do?

(*Dr Schofield*) Yes, it is, and also the French and the Dutch. If one looks at how the Directives have been interpreted, for example, the Dutch in the Contained Use Directive do not stick to the Directive's approach of having a group I and a group II classification of organisms when advising safety measures. They actually use the flexibility of the interpretation, calling things good microbiological practice, good industrial large-scale practice, which, as has been mentioned in the OECD report, have been used for many years in Europe. So other countries have used some sort of flexibility of approach to these Directives.

640. If it makes sense for the Belgians and others to react to the Directives in this way, would it not make sense for the British as well?

(*Dr Schofield*) Yes, I agree.

Baroness Platt of Writtle] Are they going to?

Chairman

641. You know what they are like!

(*Dr Schofield*) The CBI were not privy, I do not think, to all the Government's thoughts on this.

642. You mentioned the OECD a minute ago. Have you any idea why the European Community did not follow the OECD thinking on biology, which was well-known to them at the time?

(*Dr Schofield*) I have to say that I really do not know why they did not because we have always operated under a system of good large-scale industrial practice, which was reported by the OECD in 1986. Most countries in Europe have agreed with that and, of course, the Japanese, the Americans, the Australians and Canadians have also been part of that debate and produced some extremely good guidelines. They have also produced some very good guidelines on small-scale release of plants, for example, which do not appear to have been picked up by the Commission.

643. Since you believe that the Belgians have got hold of the right end of the stick—perhaps I am putting words into your mouth—are you pressing our Government to follow their splendid lead?

(*Dr Schofield*) Yes. Through our involvement in, for example, ACRE, we have been involved in specialist groups. ACRE itself is sometimes divided up into specialist groups which tackle particular questions. The CBI representatives on ACRE and in ACGM have been involved in these debates and in trying to put information through in terms of expert groups, and we as the CBI have been doing that.

644. In relation to these different interpretations of the Directives, do these differences have any effect on the famous level playing-field that we hear so much about?

(*Dr Schofield*) My Lord Chairman, I think what I just said slightly illustrates that there is not really a level playing-field. That, of course, was the intention of the Directives and it is a laudable intention that we have a level playing-field across Europe, but if I again take a little step back to the historical perspective, the Treaty of Rome asks that the objectives of the Directives themselves are interpreted into national law, which means that we do not actually have to interpret them word for word. This is what happened in the United Kingdom, the Directives were enthusiastically picked up and incorporated into United Kingdom law very much on a word-for-word basis, whereas other countries actually looked at the objectives and approached them with some flexibility. As I mentioned, things such as Annex 2, most releases in terms of Europe have been transgenic plants and a lot of the detail in 220 really is for micro-organisms. Other countries have incorporated the annexes very flexibly, which we have not done. We have 89 questions which we have to answer in our submission, which are very specific and exactly the same as in the Directive, and in terms of plants there are many that are not appropriate.

645. Does this impose a cost burden on British industry more severe than on the others?

(*Dr Schofield*) Yes, in direct cost burdens and also in terms of time submissions, time delays, but there are also costs which are not exactly hidden but they are very difficult to detail. It is in getting a product on to the marketplace. If you are the first you get a product on to the marketplace. With even a six-month lead time you will take a market lead. If you are delayed for some reason, you are tied up in bureaucracy, you are the second in the marketplace and then you are never likely to have the same impact on the market with the product. So one can see that there are a lot of different cost implications of these regulations.

Baroness Platt of Writtle

646. Are you trying to get these regulations changed?

(*Dr Schofield*) We are trying through the CBI to co-operate in putting our expert view to the Department of the Environment, who are taking the lead and are the national competent authority on changing the Directives.

647. Would you in that respect have an ally in the DTI who are trying to deregulate?

(*Dr Schofield*) Yes, certainly. We have met with the DTI and are very pleased that they have very recently set up a group called the Biotechnology Industry Regulatory Advisory Group, which is known as BIGRAG. We are members of that and it is chaired by the DTI, and it also brings together all the other regulatory people. It brings together the Department

[Baroness Platt of Writtle *contd.*]

of the Environment, MAFF, the Health and Safety Executive, the Health and Safety Commission, etc. There has only been a couple of meetings but I have found it to be very useful, very successful in actually getting, if you like, pre-notification of what is going on, so that we can be in there at the initial discussion stage and not always running trying to catch up with very late drafts of regulations, Directives and so on.

648. The problem you will have to get rid of the 89 questions is going to be very difficult?

(*Dr Schofield*) It is indeed.

Chairman

649. The regulations impose certain costs which others do not have to quite the same degree. However, that is only one cost among a wide range of costs to business. Is it a significant addition to industrial costs?

(*Dr Schofield*) Both the United Kingdom Government and the EC Commission have said that they will try to operate a one-stop shop; in other words, when you have your product which is going to go to market, it goes to one door and you place your product there and your product submission, then things will happen and you will get a notification that it is okay or not okay. If that happens—and I stress *if* that happens—obviously the costs are going to be probably quite reasonable in terms of what we have to do today to get a product to market. If, however, we are going to go through a great series of notifications under the Contained Use Directive, under the Release Directive, we have to do environmental impact risk assessments and then go through some sort of product legislation, then one can see that the costs are going to be substantially increased. If we can use, as we have done, product legislation, whether it be for medicinal products or food ingredients or whatever, and we can adopt those to take cognizance of what we are doing in terms of the technology, then the cost increase will not be significant.

Chairman: Do my colleagues have further questions?

Lord Soulsby of Swaffham Prior

650. On page 6 of your submission on intellectual property rights you do express some concern about proposed amendments. Are the examples that you give there the sum total or are there more that you would like to comment about?

(*Dr Schofield*) We are very concerned—I think my colleagues from the BSPB mentioned it—about the Legal Protection Directive. It has been very much delayed going through the European Parliament. Once again, I have to say that again it is a very good intention to have a harmonisation of patent law across Europe, but it has been very much hampered by the ethical moral debate, which has to take place I agree, but at the same time we are trying to harmonise patent law so that we can actually get products through to market or products protected across all the sectors, whether it be seeds or whether it be vaccines. If intellectual property rights are not protected, one can see that the research and development will move away from Europe to where patent protection is offered and is better. I think it is also a case of uncertainty and of delay in what is happening and the differences between what has happened in the European Patent Office, the International Patent Convention and in terms of the European Directive.

651. When you say move away from Europe to a more secure country—

(*Dr Schofield*) For example, what is happening in the United States of America.

652. It would go to the United States?

(*Dr Schofield*) One could do that, yes. One can see clearly what one might have to do. It is also the burden not only of what we might have at the moment but the uncertainty that we have in this respect at the moment.

Chairman: Thank you very much.

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HOUSE OF LORDS SESSION 1992-93

MINUTES OF EVIDENCE
TAKEN BEFORE

THE SELECT COMMITTEE ON SCIENCE AND TECHNOLOGY

(SUB-COMMITTEE II REGULATION OF THE UK BIOTECHNOLOGY INDUSTRY AND GLOBAL COMPETITIVENESS)

Thursday 20 May 1993

ADVISORY BOARD FOR THE RESEARCH COUNCILS

Sir David Phillips, Professor R Gardner and Dr R Libby

AGRICULTURAL AND FOOD RESEARCH COUNCIL

Professor T Blundell, Professor B Heap, Professor R B Flavell and Professor D Georgala

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THURSDAY 20 MAY 1993

Present:

Flowers, L.	Renwick, L.
Gregson, L.	Soulsby of Swaffham Prior, L.
Hilton of Eggardon, B.	Wade of Chorlton, L.
Howie of Troon, L. (Chairman)	Walton of Detchant, L.
Perry of Walton, L.	Whaddon, L.

Memorandum by the Advisory Board for the Research Councils is printed separately

Examination of witnesses

Sir David Phillips KBE FRS, Chairman ABRC, Professor R Gardner, Member ABRC and Chairman of the Board's Biotechnology Sub-Committee and Director ICRF Developmental Biology Unit, Department of Zoology, Oxford and Dr R Libby, Secretary ABRC, called in and examined.

Chairman

653. Good morning, gentlemen. Thank you very much for coming. We have had your written paper. First of all for the record, would you care to make a short statement introducing your position, please do so?

(*Professor Phillips*) Thank you very much, my Lord Chairman. I am David Phillips, Chairman of the Advisory Board Research Council. Richard Gardner is a Member of the Advisory Board and a Professor of Developmental Biology in the University of Oxford. Dr Libby is Secretary of the ABRC. As we say in our written submission, the ABRC has an overarching interest in biotechnology and indeed has a standing Subcommittee on the subject, which is chaired by Professor Gardner. In our view—this I think is the only thing I would want to say—biotechnology is not well regarded as a single scientific discipline, but rather a collection of techniques that have been merged from basic scientific research in molecular and cell biology and other branches of biology, which are applied variously by a wide range of scientists and technologists in academia and in industry. So it is, if you like, an enabling technology which is of very widespread use. I think that is all I would want to say. Richard I do not know whether you want to add anything?

(*Professor Gardner*) No, I agree with that.

654. Thank you very much. I think the first question we should really ask you is, what do you think is the effect of the present United Kingdom regulatory regime on contained use and general release and do you think these regulations disadvantaged research in any way?

(*Professor Phillips*) I think I will ask Professor Gardner to speak to that, particularly from the point of view of academic research and then I may add something about the impact on industry.

(*Professor Gardner*) My experience and that of my colleagues engaged in basic laboratory research is that the regulations are not restrictive. I think there is a general moan, because of the amount of paperwork in general in relation to laboratory work, through HSE and the Animal Scientific Procedure Act in recent years, but the feeling is that the regulation is about right. I think where there is very real concern, is in the domain of genetic releases, where a colleague of mine has had an application for a fairly straight forward genetic release pending for two years already. Given the current situation here, the application has to be reviewed by the HSE, by DoE and by MAFF and in this specific case it is certainly MAFF that is dragging its feet. His concern is that Canadian and American competitors are already catching up with him in this area of work and present moves in the States go towards a "30 day rule" whereby proposal for applications for genetic release it can go ahead. If they are not vetoed or prohibited within 30 days. He is concerned this will further disadvantage this sort of work in the United Kingdom.

(*Professor Phillips*) I think, my Lord Chairman, there are similar concerns in industry about the administrative time and costs spent in producing the necessary documentation concerned with the regulations. There is concern about the 60 day delay before some micro-organisms can be imported or used, which might be a significant disadvantage in the United Kingdom. There is also concern about the release of confidential commercial information as a result of the requirements to inform our colleagues in the Member States of the Community, about what is going on in some areas of biotechnology.

655. Professor Gardner, you mentioned an application going to three separate places. Does it go to these three at the same time?

(*Professor Gardner*) Yes.

656. Or do they go one after the other?

(*Professor Gardner*) No, I think they go simultaneously, because each Department wishes to look at the application in relation to different aspects of legislation. Obviously in the case of the HSE it is primarily safety; with the DoE it is the environmental considerations and with MAFF I think it is in relation to pesticides in this particular case.

657. They are really looking at different aspects?

(*Professor Gardner*) They are looking at different aspects of it.

658. When these regulations were drawn up, were you involved in any way in the discussion while this was going on?

(*Professor Gardner*) Not in the genetic manipulation discussions, no.

659. Would you like to have been?

[Chairman *contd.*]

(*Professor Gardner*) At that time my own area was more experimental embryology rather than use of genetically modified organisms. This was developed more recently. We were fully consulted in the other biotechnology area, which was human fertilization and embryology, but at the time in this area I would not have really been very much involved at all.

660. Nobody else at the Board?

(*Professor Phillips*) The AFRC was not officially consulted about these regulations at all.

661. You were not approached?

(*Professor Phillips*) No.

662. Were you a bit disappointed about that?

(*Professor Phillips*) I think it would have been helpful perhaps, had we been consulted, but I think the individual Research Councils will have been consulted. You will no doubt ask them about that when you talk to them.

Lord Flowers

663. May I ask—to go on from that—whether in other fields that involve regulation of some form or shape which effects one's ability to do research, or the cost of it or whatever, is ABRC consulted?

(*Professor Phillips*) Very rarely, if at all. If you are referring to things like fire regulations and general safety regulations in laboratories and so on, not at all.

664. It is pretty clear to me just wandering around as an interested person, that universities and research institutions are very seriously effected by health and safety regulations of one sort and another. So they should be, but very often in a fashion which does not exactly aid their research and one sometimes thinks it is a bit overbearing. There should be a voice to speak up for them and a central voice like ABRC. Why is it that you do not, or cannot perhaps?

(*Professor Phillips*) Since we have perceived the problem that Lord Flowers mentions, my Lord Chairman, we have from time to time in our advice to Government, drawn attention to these additional costs concerned with the conduct of research which really impinge on how far the science budget can be stretched. So after the event we have commented on these effects, but we have not been consulted about them in advance.

Lord Walton of Detchant

665. If an organisation such as GMAG (which is now largely outdated) is established, is ABRC consulted and would you be consulted for example with a view to nominating a member of the new group that is looking at gene therapy, for example, in treatment of human disease? Or would the Government be more likely to step over ABRC by going directly to the individual Research Councils?

(*Professor Phillips*) GMAG is now some time ago. It is my recollection that there were informal discussions about the membership of GMAG in which the ABRC was broadly involved, but I think it is the Research Councils that are mainly concerned with the support of this sort of work, which is in the front line of consultation, so to speak.

666. May I just ask whether you were in any way consulted over the formulation of the EEC Directives that relate to the issues we are discussing today?

(*Professor Phillips*) The short answer to that, my Lord, is no, though again we did express concern about the impact of these regulations since we were well aware of the impact that national regulations were already having in different countries in the Community.

Chairman

667. Did you jog people's elbows to see that you might get consulted in the future?

(*Professor Phillips*) I think, my Lord, you will have to wait for the White Paper to see what the role of the ABRC is deemed to be.

Lord Gregson] It is getting nearer.

Chairman

668. Whatever you call a straight bend! Let us come on to risk. Talking about risk in relation to this subject, how do you think risk ought to be assessed and do you think it is being done properly in Britain in relation to this?

(*Sir David Phillips*) My Lord, that is, of course, a very wide question and it embraces not only what are the actual risks of any particular procedure or activity but also what is the public perception of those risks and it is often the latter that is the more important. In my view, and I hope I am sure Professor Gardner will have much to say about this, many of the innovations brought about by biotechnology involve really very little risk at all but they are concerned with somewhat arcane areas of science and technology and include the use of words like "the genes" and so on which the public probably find rather alarming. So I think it is very much the perception of risk rather than the actuality of risk in most of the matters concerning the use of biotechnological products.

(*Professor Gardner*) We mainly encounter this in terms of group one category where we have to assess the risks ourselves and these are very low and come under the category of good microbiological practice. That is not a great problem, it is our responsibility to do that, to come to the assessment. I think, given the very technical nature of what is involved, it is the right way to do it, so long as it is overseen by appropriate committee structure to ensure people are not playing fast and loose with procedures but I do agree with Sir David that the real problem lies elsewhere. It is actually a rather strange problem because many people perceive this as rather evil tinkering with nature but that sort of tinkering with nature done in a slightly cruder way has been with us for millennia in terms of pigeon fanciers, mouse fanciers, dog breeders, all of whom who have, for no good reason whatsoever, produced, by capitalising on genetic variation and selection, the most utterly bizarre creature, for no reason at all. What the genetic procedures allow you to do is to make modifications to some purpose and in a very incisive way. I think there is this great problem with the public because the issues are so technical. It is very hard to get across the basic principles and really how

[Chairman *contd.*]

low the risks are. I think this is a real problem because when one comes on to the issue of public awareness and education, I think the prime target is schools and from a survey I conducted even six forms at very good schools are not involved in the least in this area. They know DNA makes, RNA makes protein but they are not exposed to even the most simple practical experiments in genetic manipulation that could be very easily conducted and safely conducted but it is perceived, through the regulations, to be impossible to do this, which is not the case. I think it would be quite easy to design simple and instructive experiments that they could carry out but avoiding the use of—because I think the one proviso would be avoiding the use of—antibiotic resistance and antibiotics for selection because of the general problem of exposing more people to antibiotics and possible risks associated with it. I think it would be quite possible for six formers to engage in very simple experiments that would give them a better knowledge of what this is all about. They are the future generation on the one hand and on the other hand a lot of this information is then carried from the school to the home and serves to educate and enlighten parents as well.

Lord Gregson

669. Do you think the research councils have a responsibility for guiding the educational system in the sort of procedures they could carry out?

(*Professor Gardner*) I think they could certainly offer helpful advice on this.

670. Have they?

(*Professor Gardner*) So far as I am aware this is not an issue that has even been raised, so far as I can understand. There is nothing proscribing schools from engaging in this sort of work which many people might feel is more acceptable than dissecting animals.

671. If you do not show the way who will?

(*Professor Gardner*) Agreed.

(*Sir David Phillips*) I think one answer to that, Lord Gregson, is that we have a very devolved system and there are many universities with extramural departments engaged in work in schools and many of these will involve biologists who are actually talking to people in schools. Professor Gardner himself, for example, does that.

Lord Gregson] It does not seem to have had much effect.

Chairman] I would like to get away from education back to risk.

Lord Perry of Walton

672. I would like to expand on the school side because if you are really only talking of six formers, it is leaving an enormous fraction of the public without any contact at all through families or any other way. Also it takes a long time, it is a generation almost, before it percolates through. Is there not a need for joint effort of some sort between industry and the scientific world and indeed with the blessing of Government getting together to try and make public awareness more effective?

(*Professor Gardner*) I suggest six formers are a start. It would be welcome to be more general but I think given, as was alluded to earlier, the problem of the extent to which universities are put under the microscope in relation to the HSE etc., I think if a similar thing was to happen at schools maybe it would just be ruled out on grounds of expense alone depending on how this was treated.

Chairman

673. I would like to get back to risk nevertheless. In your answer to question four, talking about safety and so on, you remark that it often happens that risks have been found to be over-estimated. Can you give me some examples of this kind of thing?

(*Professor Gardner*) I think the original work in relation to e.coli and the chances of disarmed organisms being able to repair genetic damage and then colonise was perceived as a real risk that has not materialised.

Lord Walton of Detchant

674. Can I follow that up by saying it is suggested in certain quarters that if you use such an organism or some other bacterial or viral vector from which you remove a segment of the DNA in order to splice in a segment which would be used for gene therapy, that that organism as a result becomes non-pathogenic but that if it was to be exposed in the wild to a wild type organism of the same species, its pathogenicity might be restored. Do you think there is a real risk that might happen?

(*Professor Gardner*) You cannot be dogmatic about any of these things.

675. No.

(*Professor Gardner*) I think it is most unlikely. If you look historically at the development of genetics, the rule is that the absolutely overwhelming majority of new genetic variation that turns up is at a selective disadvantage. It is a very, very small fraction of the total that are positive. It is actually fear from some of the non engineered organisms being placed in an inappropriate environment I would be more concerned about. I think a classic example is the rabbit in Australia.

Chairman

676. Do you remember the Royal Commission on Environment Pollution which commented on this subject a few years ago. Do you think the Royal Commission over-estimated the risks or dangers?

(*Professor Gardner*) I think everyone appreciated they were going in at that time to the unknown and it was the scientific community itself, I think, that behaved with great responsibility essentially calling a moratorium until people had time to take stock and see what the true situation was. It was really very unclear then. Now we have the extraordinary fact that emerged that genes operate in a very compartmentalised way, the controlled regions, the expressed regions and you can cut and splice and so long as you know the sequence of that DNA and know something about its structure, the powers of

[Chairman *contd.*]

prediction of how it will behave in particular circumstances are extraordinarily good.

677. Do you think though if the Royal Commission were considering the matter now instead of a few years ago they would be less cautious than they were then?

(*Professor Gardner*) I would hope so, it is impossible to guess but I would hope so.

678. Let us talk about Regulations again. Let us go back to our first question, the danger that the regime would prevent the exploitation by industry of research, that is not the research itself, it is the exploitation of research. Your reply is very cautious and you say that things should not be bound by redundant rules, which is quite sensible, but do you think there is a danger or not? You do not really say?

(*Professor Gardner*) I think there is a danger if you set up any regulatory organisation, unless it is party to the most recent information and development, that it will operate with a latency. Depending on how that organisation is structured, the latency can be greater or less. The truth of the matter is now in molecular biology, that an important factor in competition can be latencies of the order of months, rather than years.

Lord Flowers

679. Is it of such a nature as to put the United Kingdom at a disadvantage?

(*Professor Gardner*) I think it could well do. We emphasised in our evidence, this extraordinarily close relationship within the biotechnology industry and HEIs. Amersham, for example, now is a major player in this area and they have very close relations with, I think it is 46 of the old universities, in other words before the removal of the binary line and they benefit greatly from the quick transmission of know-how from the laboratories to them. The universities benefit equally in terms of the supply of efficient kits for saving time in conducting molecular biology experiments. I think anything that strained that relationship and made that harder, or regulations that made the industry feel disadvantaged, such an industry would go elsewhere, where the regulatory regime was suitable and that is what we have seen precisely in Germany.

Chairman

680. You say elsewhere in the paper that the United Kingdom regime is more liberal than others. Some of our witnesses have thought the United Kingdom regime was onerous.

(*Professor Gardner*) It may be onerous, but there are certainly others that are more restrictive. Denmark, for example, even self-cloning is prohibited, which is regarded as very minimal risk activity. So we sit somewhere in the middle, I think probably.

681. But not onerous?

(*Professor Gardner*) From the perspective of the basic research laboratory, I would not say onerous. I cannot speak for the commercial and industrial sector.

682. We asked you about regulations on an industry specific regime and you replied. I am not sure that I follow your reply terribly well, because you refer to Amersham International and you end up by saying: "An industry specific regime would not regulate them." By "them" were you talking about something which relates specifically to Amersham, or was that a little more general comment?

(*Professor Gardner*) Could you say that point again?

683. You begin talking about Amersham International, a well run company and end up by talking about new treatments and "an industry specific regime would not regulate them". Is that something general, or does it relate to Amersham?

(*Professor Gardner*) I think this returns to the point that Sir David made at the beginning and that is the breadth of perspective one has on biotechnology and certainly when we were addressing this issue in relation to the responsibilities of the Research Councils, you have what is narrowly defined as biotechnology and omits great areas of health care, that may involve the industry, but may also to a large extent involve technology transfer directly from the laboratory to the clinic and here the new treatments for human fertilization embryology and for genetic screening are partly of this character. There is an input from the biotechnology industry and an input more directly from the laboratory.

684. But you do not seem to have an opinion whether we want an industry specific regime or not?

(*Professor Gardner*) I think it means—"industry specific" is vague. If you are meaning a regime specific to the biotechnology industry, or if you are meaning regulations specific to each sector in the biotechnology industry, these could be interpreted in entirely different ways.

(*Professor Phillips*) I think my Lord, there is considerable merit in the present system, whereby as I understand it the Health and Safety Executive is concerned with worker and environmental safety in whatever industry is concerned. But other agencies, the Medicines Control Agency for example, is concerned with the safety of the products being produced in that industry. That seems to me a very reasonable division of labour. That sort of thing would apply across an industry in which the products are actually rather varied.

Lord Walton of Detchant

685. Lord Chairman, I think the point that is important is that there are likely to be certain developments in human fertilization, for example, and probably in gene therapy, which may bypass industry as such, by going straight from the university or research laboratory to the patient. That could not be regulated by an industry—specific process. I think that is something that we would have to bear in mind.

Chairman

686. Yes. Towards the end of the paper you make a general comment about the strong science base, or hoped for strong science base. Would you like to expand on that at all?

[Chairman *contd.*]

(*Professor Gardner*) I think this returns to a point I began earlier, about the extent to which the biotechnology industry coordinates with and cooperates with and collaborates with the scientific base and certainly the view that I had expressed from the person I talked to with Amersham, would be that were there not a strong science base in this country, Amersham would not be here. Reciprocally, there is this very real question of the strength of the industry and the provision of kits, purified reagents that are really essential for being competitive in molecular biology and if you have to go abroad for these reagents, you pay more. Very often the rule for imported products from across the Atlantic is you pay the same number of pounds sterling as the cost in the US would be in dollars, if you go to America for many of the biotechnology products. So the cost of doing science is another factor as well as the quality of it.

Lord Soulsby of Swaffham Prior

687. Lord Chairman, could I just follow up the point under 12 and the science base? You do make a very strong statement that a strong science base is necessary. Is it strong enough in this country to support a competitive global biotechnology programme?

(*Professor Gardner*) I think the answer lies in the strength of the biotechnology industry in this country and the fact that for example, the European Bio-informatics Institute, which will be a very large molecular biology data handling institute, has been located in this country at Cambridge. The decision has been made. That really offers the proof and the strength, but we cannot afford to be complacent. Molecular biology is a very expensive activity. The sort of ball-park figure that we use is that for every one engaged full-time in molecular biology in a laboratory, be they technician or post-doctor or research worker, their consumables per head are in the order of £8,000 per year now. There is great encouragement to use molecular techniques in other areas of biology, other than genetics. It is being used much, much more in ecology than in the past. So as this trend continues, so the expense of doing science will increase inevitably.

688. One of the effects of the new form of funding in universities to remove the "R" component where university people have to go to the Research Council and you will be aware of that, I am sure, it has cut out what you might call serendipity in research, where departments in fact could afford to have some of their members not funded, but doing research at a lower level of cost and the cost you mentioned for molecular biological research is such now that without a major grant from one of the Research Councils, you cannot do any research. Have you any comments on that?

(*Professor Gardner*) The dual support transfer does not technically remove the possibility of doing this. I think how people fare in operating other than through grants in that way actually depends on how universities disperse the money that was supposed to be for research prior to the transfer.

Chairman

689. We have another group of witnesses waiting. I wonder if there is anything you would like to add to what you have said before we wind up?

(*Sir David Phillips*) Perhaps I might say Chairman that the Committee may like to look at the issue of Science Magazine for 14th May which has a special section in it on Frontiers of Biotechnology which illustrates the point I began with that the word biotechnology covers a multitude of activities which are of increasing relevance to an extremely wide area of science. You will find biological techniques, these techniques, being used in almost every area of biology, for example, in neuro-biology and environmental science as Richard as said, everywhere. So thinking of it as one unified activity tends to give one the wrong impression.

Chairman] I think we are beginning to gather that. Thank you very much. If you have any second thoughts please let us have them.

Memorandum by the Agricultural and Food Research Council is printed separately

Examination of witnesses

PROFESSOR T BLUNDELL FRS Director General, PROFESSOR B HEAP FRS Director of Science, PROFESSOR R B FLAVELL, Director of Plant Science Research and PROFESSOR D GEORGALA CBE Director of Food Research, Agricultural and Food Research Council, called in and examined.

Chairman

690. Good morning, gentlemen. I wonder if you would identify yourselves for the record and tell us something about your organisation. If you care to make a short statement outlining your stance in these affairs we would like to hear it.

(*Professor Blundell*) Thank you very much, my Lord Chairman. May I introduce myself, Tom Blundell, I am Director-General of the Agricultural and Food Research Council. On my left is Professor Brian Heap who is our director of science and also director of the Babraham Research Institute concerned with animal physiology and genetics. On my immediate right is Professor Flavell, he is director of the John Innes Institute and the Institute of Plant Sciences which is at Norwich. On my far right is Professor Georgala who is director of food research in the AFRC. If I could take the opportunity, my Lord, to make a short introduction and to begin on behalf of the AFRC by waving in front of you a world document which is produced by the OECD on biotechnology agriculture and food. This document, which reflects all of those countries in the OECD's views on biotechnology in this area, was written to a very large extent by members of the AFRC on personal invitations and three of the authors of chapters are with me today. That is just to reflect on the fact that almost all of the AFRC's activities, whether they are in micro-organisms, in the plant area or in the animal area depend in their basic science on new developments in biotechnology and genetic modification. Of course, all of the opportunities for application of our research, whether it is in the pre-farm gate area of agriculture, in livestock or crops, or whether it is in food processing, will depend very much on biotechnology. We see biotechnology as the central part of our technology transfer. It will contribute all the way through from crops and livestock to food products but I would also like to emphasise that biotechnology is central to diagnostics, for example for gauging nutrient levels or pest levels on the farm and of course looking at pathogenic micro-organisms and other problems for food safety further along the chain. So both in products and in diagnostics it is absolutely central. Finally I would like to say that not only is our science itself very much dependent on the new areas of biotechnology but we have sporned a number of spin off companies and I believe you have already seen ABC—Animal Biotechnology Cambridge—and the AGC—Agricultural Genetics Company. Both these small biotechnology companies have derived in a very large way from the biotechnology arising from our organisation and we value very much this and other opportunities to transfer it into the broader area of application which we believe will underpin much of the competitiveness of biology-based industries in the future. Thank you very much.

691. That OECD publication you mentioned, was that published last year?

(*Professor Blundell*) It was. We had a formal presentation of it a month or two ago in a press conference.

692. It is pretty well up to date?
(*Professor Blundell*) It is.

693. In the summary in your written evidence you are fairly critical of the United Kingdom regulatory regime which you describe as "onerous" and you suggest that a vertical product based regulation has advantages. I take it by that comment you prefer vertical regulations to horizontal, if I am right I wonder if you could tell me?

(*Professor Blundell*) If I could begin by responding to that question, my Lord, by saying that, as one develops an area of biotechnology in a strategic sense then any regulation has to be horizontal because the specific product is not identified. As we move towards transferring our technology into specific products, then we believe that the regulations should become increasingly vertical or product-orientated. I may ask Professor Georgala to build on this from the food end.

(*Professor Georgala*) Yes, my Lord Chairman, surveying it shows food is one major outlet for biotechnology in primary production and processing. One can see enormous differences in the technologies actually used as the products stream up towards the marketplace both in the processes that have been applied and in the way one would approach the risk assessment and possibly even issues such as labelling down the road. I think for that reason, as far as food application applies, I certainly see the product by product assessment as a desirable approach. In fact that is a United Kingdom stance at the present time and I think it is also developing in the EEC Directive on Novel Foods.

694. So horizontal stops at the lab door?
(*Professor Blundell*) We would not say it stops.
(*Professor Georgala*) At some stage, in fact, in terms of release and application in the environment, as you move into the use of materials and individual process regimes, the peculiarity of those needs special attention.

Lord Wade of Chorlton

695. Could I follow up and put a point of view on it. Clearly when one hears the evidence it makes sense it should be the final product that decides whether it should be within the project or not and the vertical approach, as you suggest, sounds the most common sense one. Yet we have received a lot of evidence to the fact that one of the greatest concerns about biotechnology is the perception of the public. There is a wide gap between what scientists know and what the public understands. This has ever been thus with a new product. Is not one of the ways that these fears will be overcome by people to actually eat and consume products which they know to be produced by biotechnology and yet they are still fit and well and

[Lord Wade of Chorlton *contd.*]

it has had no impact on them? If we protect them from the knowledge that products are coming out on to the market place and have in fact been produced by biotechnology processes, are we not continuing this gap between the fear and the reality? Is there not an opportunity or a need to actually let the public understand that there are products on the market that are made as a result of the biotechnology process but in fact are harmless to them, they are used effectively, they save their lives, they feed their bellies and they make them feel better? Is that a view that we need to look at more positively, or not?

(*Professor Blundell*) I should say that the AFRC is very concerned in an active way about public perceptions and acceptability and we are certainly aware that know-ability is a very major factor in the public perception of risk concerned with biotechnology. I believe that we have to be quite straight forward with the public in this area, otherwise we will loose their confidence. So I agree with you in general. If I could just lead away from your question to say in general how we are viewing the question of public perception, because I think that it is going to be most important in terms of the implementation of the results of new biotechnology and also of course in the development of regulations in this country and EC wide. We have a three—pronged approach to the question of public perception and this really emphasises firstly, the research area. We are doing research—and I will ask Professor Georgala to say a few words on this—into consumer attitudes and public perceptions. Secondly, we are interested in education and biotechnology and the development of perceptions. Thirdly, we are interested in direct interactions with the consumer and perceptions. If I could just make a comment on the latter? We are now moving ahead with Professor John Durrant in introducing "consensus conferences", which were first developed in Denmark, for the area of biotechnology. In these one involves the public in a quite intense process of discussion and thinking about areas of biotechnology and then allows them to come to a decision about biotechnology applications. This is quite an expensive operation, but quite an important one in developing our understanding of the public's perceptions and also having some effect on perceptions themselves. If we could move to the subject of consumer involvement and ask Professor Georgala just to comment on how he is approaching this.

(*Professor Georgala*) Yes, my Lord Chairman, we identify this as a major issue. Even when the regulatory position is well developed, it is still clearly evidenced from our contacts with the consumer interests that there will be concern about trust and belief. We have taken a significant initiative with the National Consumer Council and our Institute of Food Research to hold joint workshops to explore with consumer interest groups, the boundaries and issues as perceived from the consumer interests side and from the scientific side. We are sharing views and we see that as one major step forward, actually sharing information about where the science is going and what are the consumer assurance issues that we need to attend to. As part of that, we have also taken a research initiative. We actually have set up a consumer science department in the Institute of Food and Research, funded by AFRC and we have a research programme funded by MAFF in that department. We have been exploring with ordinary consumers some of the perception issues relating to biotechnology. These are giving many of the signals we will have to address. For example, one of the problems at the moment is that many people do not have an actual issue that they can address. There are not many biotechnology food products they can actually go and recognise and decide about. The attitudes that have been struck at the moment are based on a lack of knowledge of what is going to appear in the market place. That is the first thing. The second thing we are identifying is that the views on risks are not extreme. They can be addressed by sensible exchange of information and by the development of trust in the Government's regulatory procedures. Where we are finding it of course, is that one of the key issues still is the view individuals have about the amount of control they have over their food choice and I think that will bring us ultimately to questions of labelling. In this area, it is different from, for example nutrition, where individuals believe they have control over their choice of diets. In this area there is a belief that they lack control and that society and Government will have to be a major player in that.

Chairman

696. Would you like to say something about labelling? How would you do it?

(*Professor Georgala*) I happen to be Deputy Chairman of the Food Advisory Committee, that is the Government's Committee that advises on labelling and that subject is now part of a major consultation exercise widely within industry and with consumers. My personal feeling is that labelling may have to play a role. This is a major consultation—you may have seen the paper from the Food Advisory Committee—and what we tried to do there was to tease out, whether in the consumer's mind there is a blanket fear about the whole area of biotechnology, or one can segment out areas where labelling may be less important. I take two extremes: One is, does one have to label refined sugar as being processed out of a plant that is genetically manipulated, as opposed to labelling say a yoghurt that is made and still has a live GMO in the yoghurt? The Food Advisory Committee will be trying to tease that out and when that becomes clearer, I think Government will be in a better position to decide on the labelling policy. I think we scientists need to be very sympathetic to the possible need for labelling in certain areas.

697. In fact you might lean towards what you might call "over-labelling"?

(*Professor Georgala*) I would be cautious, because our own research evidence is also that labelling can frighten. It is a very difficult balance. Our own research in the institute shows that any labelling phrase that we use at the present, has a negative connotation.

Lord Flowers

698. Could you not be forced into labelling by your competitors, who are using natural products so to speak, saying: "These products do not contain GMO derived substances."

(*Professor Georgala*) That may well happen, in fact. We have seen that in early debates about food additives.

Lord Whaddon

699. There are within the food industry some well known vested interests. Do you find that their pressures are obvious in your work?

(*Professor Georgala*) Not in my Institute, my Lord Chairman. We operate as an independent institute and we keep our minds very open with the consumer world, as with industry. I do not think industry (in my own impression) would be at odds with us to reach some sensible position that allows the technology in the products. The problem is that in food there has not been a tradition of labelling the process whereby food is made. There are very, very few foods you actually see on the label, process information. The label is only a limited size. There is only a limited amount of information you can get on it and that is one of the problems. I do believe in this area that sensible labelling may in due course, in certain areas, help the industry and consumer acceptance.

Lord Walton of Detchant

700. In relation to the issue of public perception, are you represented on COPUS (the Committee for the Public Understanding of Science) and I would be interested to know how effective you think that is proving to be? Following on from that, may I just raise with you the question of the EEC Directives, where we have been given to understand from several quarters that the Directives in relation to this field were originally likely to be quite acceptable, because of the advice given by scientists to others, but that when they reached the Council of Ministers in the European Parliament, the environmental lobby was successful in making them far more rigid than was originally intended. If you feel that—and it is clear from your paper you do—what is the avenue through which you can make representations to Government to see that they might ultimately be modified? Is it through the AFRC, or can you go direct and if so, to whom?

(*Professor Blundell*) My Lord, that is an extremely complex series of questions. May I go back to the first one, which was on COPUS and say that we do not have a direct involvement, although as a fellow of the Royal Society and as a Member of ABRC, I have many interactions with it and at the AFRC we have given it what support we can. I think it is important for COPUS to be able to identify areas where useful work can be done. Many of the areas of our own research are relevant, for example we have two projects in schools, one on perceptions of biotechnology and another to look at education in biotechnology. We are very happy to interact on such projects with COPUS. You were asking us a much broader question also about EC directives and perhaps to get a view on that I could ask, first Professor Flavell to give some of his experiences on the plant side and then we could move to the animal side afterwards.

(*Professor Flavell*) Gladly. I too understand that the environmental lobby in Europe had a much stronger influence in the drawing up of the final documents in the EC Directives than would have been the case in some Member States but I cannot be more specific than that in detail. When it comes down to a Member State legislation based on those Directives, there clearly were difficulties because the original EC Directives were not particularly well formulated on scientific grounds for the range of applications that are likely to take place in Member States. So there was further room for misrepresentation of the best sorts of guidelines and there is something of a history of that within the recent United Kingdom legislation. Routes to influence? We did have an opportunity, as did many others, to interact with the Department of the Environment in the framing of the recent legislation and we took that opportunity and we think we had a significant influence in getting the United Kingdom legislation into a form that was at least more appropriate than it was in the first drafts taken from the European directives.

(*Professor Blundell*) Professor Heap?

(*Professor Heap*) My Lord Chairman, thank you, the area of animal production is one in which AFRC have considerable research investment and is a topic that was the focus of concern within the EC in the formulation of legislation and continues to be from the point of view of the impact of introducing genes into species where there may be an impact on animal welfare. So in terms of our discussions and inputs, this has really been through the Law Society who spent considerable time in formulating recommendations for the legislation which was compiled by the Department of the Environment. We had very considerable interactions with them in discussing particularly the basis of the risks and the benefits that could be perceived from developing this area of science. The three aspects, of course, which we focused on especially were the impact of introducing genetic material into farm animals, the way in which that might have an influence on those who are involved in the research itself (that is the research operators), the possibility that there may be an influence on the animals that would be detrimental in terms of welfare and whether there was any possibility that there was an influence in terms of environmental considerations. So in all those areas we have had some considerable discussions in the formulation of the legislation.

Chairman

701. Despite the influence which Dr Flavell identified in regard to the Department of the Environment, you still regard the United Kingdom regime as harsh or onerous?

(*Professor Blundell*) Yes.

702. You go on to ask for fast track procedures in the United Kingdom similar to those which prevail in the United States, can you tell us something about that?

(*Professor Flavell*) One of the features which is particularly onerous in the direct implementation of the regulations, as they were first formulated, is the

[Chairman *contd.*]

very large body of evidence that you have to amass on every submission for permission to release a genetically modified organism and very often one finds oneself going over the same ground because the biological host and the genes being inserted have been released. In the United States, they have come rather rapidly to a position where crops which are extremely well understood in terms of their agricultural behaviour and interactions with the environment, have been taken as read in terms of most of the issues and classes of genes that have been inserted into them, that can be understood in adequate risk assessment terms, have also been categorised. So when it comes to making proposals, the whole process is simpler, it is faster and it is less expensive. In the United Kingdom legislation there were some declared opportunities for streamlining, not along the same lines as in the US but similar and it is those that I think we really must encourage to be adopted because they are logical. There is no reason why failure to adopt them, in my view, significantly influences risk or the risk assessment process and it is building upon a case by case knowledge base. So, if we can streamline then perhaps the regulatory system would be far less onerous and much better tuned to the position of competitiveness that we would want to adopt in relation to the United States.

703. You are telling me that the less onerous regulations in the United States would be satisfactory if they were applied here?

(*Professor Flavell*) One can debate the fine print of such things—

704. Yes.

(*Professor Flavell*)—and I would not want to say at all that I think the US regulations are ideal but I do think that where there is sound scientific logic and acceptability by a broad section of those who look at them and that there are not significantly enhanced risks associated with a range of products then there is no reason in legislative terms to create an expensive onerous process that gets in the way of so many things. I think it is very probable that with the right streamlining and interpretative process the United Kingdom guidelines could become perfectly satisfactory from this point of view.

705. You would like to move a bit towards the American system?

(*Professor Flavell*) Yes.

(*Professor Blundell*) Whereas, my Lord, we find the system onerous, we do recognise that we are in an intermediate position internationally between some European countries such, Germany and Switzerland who have much stricter regulations and the rather more straight forward situation in the United States. We are not saying ours is the most onerous.

Chairman] No. I think the Germans would probably agree with you.

Lord Wade of Chorlton

706. Is there any reason for you to believe that in fact where the regulations have been less onerous they have been in countries where the industry is more important from an economic point of view and been more onerous where it is not an important industry anyway and is not likely to have a big impact one way or the other on the economy?

(*Professor Blundell*) I would have thought the evidence for that view is not terribly strong because the German biotechnology industry has tremendous potential. They have a good science base, they have a large number of very large pharmaceutical and chemical companies that could build on a biotechnology base and indeed have tended to. So I think it has not been to the advantage of German industry and we have seen indications of German industry moving their science base to the States. So I do not think there is any strong correlation. The Swiss industry is also extremely strong and they have quite strong regulations. Of course, there is a great deal of concern about onerous regulations in industries in those two countries.

Lord Whaddon

707. Presumably your scientific colleagues in Germany and Switzerland have similar points of view to your's to their problems, why have they failed?

(*Professor Flavell*) They have been failing for a long time inspite of very rigorous representations. I can only relate to you what I have learnt from them and that is, more so in the past than at the present time, the radical extremes of the Green movements, which have been politically strong and had influence on politicians there, had a stronger voice in legislative terms than the scientific community.

708. I have heard it said that it was the small farm lobby that was also very active. Have you any reason to think so?

(*Professor Flavell*) I do not have specific information on that point.

(*Professor Heap*) This is important point to consider in relation to Switzerland, where of course there are a very large number of small farmers. This became very clear, for example, in relation to the possibility of introducing bovine somatotropin, a genetically engineered product which increases milk yield, about which there have been very considerable reservations, particularly in mainland Europe and also in Switzerland. This was because of the potential impact on the small farmer unit and the possibility that it might lead to a decline in the numbers of small farmers. Yes, there is a very important socioeconomic component in that discussion.

Lord Soulsby of Swaffham Prior

709. Could I follow up on the question of regulations and ask what degree of reciprocity is there between national requirements or Community requirements in other countries and also what should it be, if it does not exist?

(*Professor Blundell*) My Lord, I am not sure I fully understand the question in terms of reciprocity.

710. In terms of regulations, for example in the USA, you have a product produced and it is licensed in the USA, how much of the regulation can you lift from the USA situation to apply to United Kingdom?

(*Professor Blundell*) Within the European scene, where it is much more easy to answer, we believe that

[Lord Soulsby of Swaffham Prior *contd.*]

a level playing field is desirable, both with respect to competition at the basic science level and at the industrial level. Even within the European Commission area, we are worried that within the European Directives there are different ways of interpreting the Directives that depend on the Authority in the particular country and that is going to depend on public perceptions and political strengths.

Lord Walton of Detchant

711. On that point made by Lord Soulsby, which is very important, if a product produced in the USA, according to their less onerous regulations, were then to be produced for marketing in the United Kingdom and it was not shown to meet the much more rigorous United Kingdom regulations, would this prevent it from being marketed here and vice versa?

(*Professor Flavell*) Well, I make one or two points. The regulations in terms of acceptability of the product might not turn out to be too different. The process by which you have to gain that may turn out to be very different. Clearly, the questions you are raising are at the heart of some huge difficulties about harmonisation of acceptance, but I think we have to also realise that particularly in the agricultural sector, where it is a worldwide business and products are moved around in trade, that something which gets produced in one country, is almost inevitably going to end up somewhere else, either as a seed and grown, or in some kind of product. So there is a major formal problem in terms of regulations and a huge practical problem of how could you stop the adoption and use of a product in one country versus another? In the Member States of Europe, I understand that the situation is that if a product is accepted in one country under the appropriate Directive, then it has to be accepted by all Member States, unless in the example of the release of a genetically modified plant or organism, there is something special about their geographic environment that would pose a risk separately there. But in view of what I said earlier, you can see that it is almost a meaningless situation with respect to real containment of any risks that are associated with any kind of product.

(*Professor Georgala*) As far as food goes, any food sold in this country has to meet the requirements of the Food Safety Act 1990. So I think whatever country it comes from, it has to meet a primary requirement by the producer and the seller of safety. Where there may be a international differentiation then is on the labelling issue. If in fact in one country labels are required that would be a decision for the exporting country, whether they wished to label in that other country.

Lord Soulsby of Swaffham Prior

712. I was just going to go back to the point you were making about the onerous nature of the regulations and the documentation. Can you use documentation and evidence on biotechnologically developed products, in the same way as I think you can with other regulations? You used to have to do it all in your own country, once upon a time. Now you can use information derived from elsewhere. Is this possible in regulations pertaining to biotechnological products?

(*Professor Flavell*) You could certainly use the information. The format is somewhat different, because at the present time, in submissions to underpin the United Kingdom legislation, one responds to a specific series of questions and therefore one is putting the data into a different form than would be required in the United States, but clearly the base information is the same. One of the points that we were attempting to press upon the Department of Environment was that we would hope that both the regulatory authorities and indeed those submitting the information, would have open access to the risk assessment material that was available around the world and that it would be acceptable as evidence, to stop reinventing the wheel and making every institution bring in world experts to reassemble the base information.

Chairman

713. You find these regulations bothersome, clearly? I am wondering just how much it matters. As you say, the regulations impose certain costs on your industries, but there are a great many other costs imposed on your industries from a variety of sources. Are the costs imposed by the regulations significant, or are they merely marginal?

(*Professor Blundell*) If I could, my Lord Chairman, start at the project level in the university, then we can see that we operate on recurrent expenditure for a genetic engineering project of about 8,000 a year. If one is going to have to pay—

714. Is that £8,000?

(*Professor Blundell*) £8,000 per year is the total recurrent cost of a genetic modification kind of experiment for one person. Then the cost of each release at £1800 begins to look a very large proportion of the funds available. This gives only very limited flexibility in an individual project, although there is slightly greater flexibility in an institute. I think I cannot comment on the industry, but maybe others would like to have a go.

715. It is significant at the university level?

(*Professor Blundell*) It is very significant in the area of the science base.

716. Now industry?

(*Professor Flavell*) I was going to add one more thing about the science base, because I think it is very important. The strength of the science base is to some extent proportional to the number of graduate students and so on, who are initiating the innovative aspects and I have no doubt at all that if the whole business of gaining permission for release remains as onerous and expensive as it is, then those will be real limitations on the width, strength and depth of the innovative science base in the United Kingdom. Your point about industry is correct I am sure, in that the costs in the plant area are not great in relation to the total costs. However, one comes back to two features which pertain to the implementation of the regulations. In order to sustain a plant breeding business one will have to submit a large number of separate applications that would have to be run simultaneously. This multiplyies the number of

[Chairman *contd.*]

several thousand pounds. A second feature is time. One runs these sorts of developmental processes on an annual cycle that is fixed by the environment. So, if you have a regulatory system that is onerous you can easily lose a whole year and that is where competitiveness comes in. So I am sure that the key issue in industry is not just costs seen in the single sense but, it is the proliferation of numbers of applications—

717. Somebody might get in first?
(*Professor Flavell*) Precisely.

718. Some foreigner.
(*Professor Flavell*) Where patenting is involved which determines the whole future value of the novelty, arriving there first at the point where you can justify the patent is of course a key financial aspect.

Lord Wade of Chorlton

719. Do you believe the regulations are actually preventing the commercialisation of many products, preventing venture capital that might develop products more effectively and actually existing businesses being not encouraged to move into this area that should be?
(*Professor Blundell*) I think, my Lord, a lot of the uncertainty in the investment in biotechnology comes from the uncertainty about how regulations will change in this country. Many people, for example, do not realise that organisations like Greenpeace are totally opposed to all biotechnology in the genetic engineering sense. We can even see within university laboratories young scientists doing recombinant work all day and subscribing to Greenpeace out of their small grants. There is a tremendous pressure that we are all aware could increase and that certainly leads to a great deal of uncertainty about investment. I think it is that sort of level rather than the immediate problems of developing products.
Lord Wade of Chorlton] Uncertainty about what might happen.

Lord Renwick

720. May I ask, we heard earlier in evidence that there was some danger of disclosure in going through the regulatory process, that innovatory processes might be disclosed to this. Is there a danger in any of these groups?
(*Professor Georgala*) My Lord, certainly not at the food end. The applications to the Advisory Committee on Novel Foods and the business of the Food Advisory Committee is confidential in the detail. I do not think there has been evidence of that being a problem at the food application end.
(*Professor Heap*) I think that is also true in the animal field, bearing in mind, for example, the requirements of the Home Office Regulations where one has to identify for the Home Office inspector the intention and the plan and the detail of the experiment. That is carried out under the existing legislation and I have not detected a problem of the type that you suggest in the way it is enacted.

Chairman

721. You people deal with plant and animals.
(*Professor Blundell*) And micro-organisms.

722. I was just going to come to micro-organisms, thank you very much. The original EC draft Directives were aimed at micro-organisms I am told. Is that a fundamental flaw and if it is a flaw in the Directive, how do you think it could be ameliorated?
(*Professor Blundell*) Our view, my Lord, would be that the initial regulatory reaction to plant and animal biotechnology was based on that for micro-organisms; of course that is where the experience came first. But the general view I think of all of my colleagues here is that we have developed a little beyond that now and the regulatory authorities are well aware of the particular challenges on the plant and the animal side. So that may have been a problem but it is probably not a present difficulty.
(*Professor Heap*) I would agree with the Director-General's comments.

723. You think it will be ameliorated without further direct pressure, amelioration is on its way?
(*Professor Blundell*) Yes.

Lord Perry of Walton

724. Could I ask whether that amelioration, which we all think must come, can come without changing the EC regulations through the interpretation the British legislation puts upon them?
(*Professor Blundell*) Our views, very much as Professor Flavell outlined a moment ago, are that amelioration can come from experience of working in these areas and through a simplification process where analogous operations within a particular institution can be brought together to minimise the number of separate applications. It is that kind of simplification that is going to help tremendously.

725. There is no real pressing case for trying to have a British initiative to have the EC Directives changed?
(*Professor Blundell*) My own view is that, as with micro-organisms, it is wise for scientists to be precautionary at the beginning and to make sure that there are no administrative hurdles. They must show by evidence of activity in the area that the dangers are perhaps being over-stated and then the regulations can be eased off. We have seen that certainly with micro-organisms. Over the past years we have been able to ease the restrictions in almost every laboratory.

726. Yes I agree but the easing off can take place either through British departments or it could be done through the EEC?
(*Professor Blundell*) Correct.

727. My question is will it be enough simply to ease off through British interpretation of the Directive or will it be necessary to have the Directives modified?
(*Professor Heap*) Obviously it is going to be necessary to have a clear representation of what the British intention would be in this connection. I would like to reiterate the Director-General's point in relation to streamlining and whether it is going to be necessary for us to develop a specific British initiative

[Lord Perry of Walton *contd.*]

to do that. I think we would have to take advice in that area and I am not sure that we are best placed to formulate a view. That would be my own position.

Chairman

728. We are told, for example, that the Belgians interpret the regulations with a fairly light hand, is that not a more sensible way of going about it rather than re-writing the whole rigmarole?

(*Professor Blundell*) I think this sums up our view at the present time. That was my point by saying that the competent authorities within a single set of directives in Europe do treat regulations in a slightly different way.

729. There is something in your paper I would like you to tell me about, you refer to the PROSAMO project—the Planned Release of Selected and Modified Organisms - which is now underway funded by a variety of people. Could you explain something about that to us?

(*Professor Flavell*) The project was initiated for two or three reasons because industry and the AFRC and the research base was concerned about some of the scientific issues that were being raised in relation to risk assessment of genetically modified organisms. Industry felt perhaps they were in something of a conflict of interest situation and were very keen to see some independent research done by universities and AFRC institutes and it was at a time when the regulatory committees were feeling their way about how to come to consensus decisions about the release of organisms. One of the most sensitive areas in plants concerned out-pollination to other plants of the same species that were growing nearby but which were not genetically modified and therefore not subject to the legislation. Because of the natural process of pollination by genetically modified organisms theses organisms would become genetically modified in spite of being out there already in the environment and therefore not subject to the process of release. The research that has been done since 1987 in my Institute has focused on potatoes and oil seed rape. The question of the frequency of pollination carried out by bees has been the focus of study to address questions such as how far does pollen travel, how far is it carried by a bee and, what is the efficiency of out-crossing to other plants of the same species and related species. Data have now been gathered on these points, within the constraints of the given experiments and it has already been communicated to the Advisory Committee for Release of genetically modified organisms. I understand that they welcome the information because that kind of information was not known before. It does help them get a more mature view of the issue of cross-pollination, but I think everybody accepts that because this is biology, the experiements do not give a precise answer. So, it does not make a qualitative difference to risk assessment, but it provides more comfort and understanding. I would add one more point, Lord Chairman, and that is that I think those series of experiments and all the discussions that have been associated with them in the research base and within industry internationally, have brought this whole issue to a much better level of understanding, far beyond the confines of the particular experiments. In that sense I think everybody involved feels they contributed richly to awareness and maturity of handling of the issues.

Lord Gregson

730. Both those experiments concerned crop situations, whereas there is no natural potato in Great Britain, there is no natural oilseed rape in this country, so they are not really releases to the natural systems are they? They are releases to other crop systems. Is there not a difference between the two?

(*Professor Flavell*) Very much so. There are species related to oilseed rape that are indigenous in the United Kingdom and cross-pollination occurs. Consequently this particular example has received a great deal of environmental attention. Other experiments have been done, spearheaded from Imperial College, which have addressed the issue in relation to indigenous species, for the reasons that you raise. It is a very complex subject. It perhaps should be noted by one and all, that many of the crop species that we use in the United Kingdom did not evolve here and do not have close relatives. This is very helpful in relation to risk assessment, but of course is not often recognised by people who look at the issues in a casual way.

Chairman

731. I must say, I hope your experiments into the potato lead to a bigger and better Kerr's Pink!

(*Professor Blundell*) Could I add to that by saying that in the AFRC we believe we have a responsibility to carry out research which is relevant to ecological assessment? There is quite often an apparent divide seen in research between research which is leading to exploitable products, for which of course we are very well recognised, and the research which might be seen to be underpinning the regulation. It is my view that within the Council Institutes and university projects, we should be sure that we integrate the ecological assessment, which means that as one is doing the plant genetics, for example, one needs to bring alongside the morphology, the taxonomy and the ecology. We must be sure that we have expertise in these areas and we do carry out experiments relevant to the broader area of ecological assessment in parallel and integrated withthe genetic modification. It is not just a question of regulating at the end. It is a question of understanding the whole system of the new biotechnology as we progress to the new transgenic plant or animal.

Chairman] We will make this the last question.

Lord Soulsby of Swaffham Prior

732. Lord Chairman, I just wanted to deal with the science base, if you do not mind, under question 12 and I was delighted to hear Professor Flavell say, if I heard him right, that the health of biotechnology related to the number of graduate students and post-doctorals in universities and I am aware that the AFRC has been putting a greater amount of its funding into universities by way of research grants and graduate students and things like this. Traditionally the AFRC has chosen to place its

[Lord Soulsby of Swaffham Prior *contd.*]

major funds in its institutes compared with the Medical Research Council where much of its funding has gone into units in universities up and down the country and possibly provided a greater mobility of research in this way. Has the AFRC perceived any change in its policy of supporting its major institutes as opposed to the policy of the Medical Research Council or do you think that you have got the proportion and the formula about right?

(*Professor Blundell*) First, my Lord, I would not see the distinction between the MRC and AFRC in quite such a clear way. MRC, of course, still has a large investment in its institutes, indeed it also has a large investment in units which we do not have. We, like the MRC, see the importance of a mixed economy of large facilities where we can have, for example, category B containment facilities within an institute for certain transgenic systems, together with small project grants where we can exploit an expertise in a particular plant that was not within any institute. So we see that in a mixed economy, a competitiveness and new opportunities come from the mix of different structures. The health of the AFRC will certainly be in keeping all of those components alive. I am sure they all are at the present time contributing towards biotechnology in plants and animals and organisms and will be important in the future. In fact we have moved our funding away from the institutes to increase investment in the universities. Our investment in the universities is complemented by the biological sciences funded by the SERC and this needs to be seen as a whole. We have a very large investment at the present time in universities and it provides a good basis for flexibility and new opportunity.

Chairman] Thank you very much. If you have any further second thoughts or even third thoughts we will be quite happy to receive them in due course. Thank you very much for coming.

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SESSION 1992-93

MINUTES OF EVIDENCE
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(SUB-COMMITTEE II REGULATION OF THE UK BIOTECHNOLOGY INDUSTRY AND GLOBAL COMPETITIVENESS)

Thursday 27 May 1993

SCIENCE AND ENGINEERING RESEARCH COUNCIL

Sir Mark Richmond and Dr D Clark

ADVISORY COMMITTEE ON GENETIC MODIFICATION

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HOUSE OF LORDS SESSION 1992-93

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THURSDAY 27 MAY 1993

Present:

Gregson, L.	Platt of Writtle, B.
Hilton of Eggardon, B.	Renwick, L.
Howie of Troon, L. (Chairman)	Wade of Chorlton, L.
Perry of Walton, L.	Walton of Detchant, L.
	Whaddon, L.

Memorandum by the Science and Engineering Research Council is printed separately

Examination of witnesses

SIR MARK RICHMOND FRS, Chairman and DR D CLARK, Deputy Director—Programmes, called in and examined.

Chairman

733. Good morning. Thank you very much for coming. I do not know whether it is appropriate to ask you to describe the work of the Science and Engineering Research Council today or not.
(*Sir Mark Richmond*) We can still describe it today!

734. Tell us for the record something about yourselves and about the Council and your attitude towards this matter.
(*Sir Mark Richmond*) We are a Research Council responsible for funding a lot of work in universities in physical sciences, engineering, mathematics and biology and within that compass comes, at the moment, the funding of a considerable amount of biotechnology. As you imply, the White Paper yesterday indicates some changes.

735. These changes will be quite serious, I take it?
(*Sir Mark Richmond*) They will be significant. I think the White Paper actually uses the word "significant". There is to be a Biotechnology and Biology Research Council and presumably therefore transfer of responsibilities and funds from the existing SERC to that new Council.

736. So that the work of this Enquiry will still be somewhere within the remit of these two?
(*Sir Mark Richmond*) Yes.

737. I wonder if you could tell me whether the regulatory regimes on GMOs has had any effect on the work of the SERC?
(*Sir Mark Richmond*) First perhaps a word or two about the SERC's support of work in this area. We are, I think, predominantly concerned with the sort of work which is covered by the arrangements for retrospective approval. We are not much involved in release. So I think, if you are to use a vernacular phrase, we are at the down-market end of this and therefore I think of the regulations which are proposed. They of course have some effect on us, but they do not bear quite as strongly on our constituents as would be the case if we were working at the more hazardous end.

738. It is not too severe on you?
(*Sir Mark Richmond*) I think the feeling at the moment is that it is not too severe.

739. So you would not be pressing for changes in the regulations?
(*Sir Mark Richmond*) Not I think specifically for changes in the regulations. I think there are things that do concern us. One is that the regulations should not be tablets of stone. Things do change and I think one would want to see written into regulations—I am a great believer in the need for this: certain clauses and devices for periodic preview on change. In the time I have been involved in biotechnology, I have seen perceptions change very considerably and one has to accept that the regulations do reflect perception very strongly.

Baroness Platt of Writtle

740. Do you mean by that, public perception, or perception within the industry itself?
(*Sir Mark Richmond*) Both I think. Perhaps this is more evident in other countries. My judgment would be that public perception has had a very big influence on regulation. Public perception does not equal, but to a certain extent relates to, politics; and the politics lead to the regulations. I think public perception does change and therefore I do not feel the regulations should be tablets of stone.

Chairman

741. We are told that the implementation of these regulations varies from country to country?
(*Sir Mark Richmond*) Yes.

742. Places like Germany and Holland and so on are quite severe. Belgium seems to be rather flexible and Britain is presumably somewhere in the middle. Would you like Britain to stay in the middle, or move towards one or other of these extremes?
(*Sir Mark Richmond*) I think one would obviously want to be in the middle. I think that is a prudent position to be in, in most things. As far as we are concerned—I am stressing I am talking on behalf of the SERC—I do not think these arrangements are massively intrusive. Most of the necessary arrangements in terms of containment are already in place. A lot of the approval is retrospective. Were I speaking from the point of view of the Medical Research Council, and perhaps the Agriculture and Food Research Council, I would be saying rather different things.

743. I wonder if you could tell us something about the assessment of risk. There is a sort of formula, I

[Chairman *contd.*]

gather, through the HSE, which is widely used. Are you involved in this in any way?

(*Sir Mark Richmond*) Perhaps I should say again our position is rather different from, for example the Medical Research Council, in that we basically respond to bids from universities to do work. Therefore we have, I think it would be true to say, no facilities ourselves—

(*Dr Clark*) That is right.

(*Sir Mark Richmond*)—over which these regulations would operate and therefore we are one degree removed. So that is the background to the SERCs position. The question of the regulations, I just now draw personally on my experience, because I was on the Genetic Manipulation Advisory Group for a number of years and was actually rather heavily involved in drafting the first set of regulations that were published in the United Kingdom. All the way through we have been, in this area, between the upper millstone of public perception and the lower millstone of what the real risk is and the difficulty is to establish the real risk in an objective way, which has always been difficult. I think all the schemes that have been developed are approximations. So just as I would not want the regulations to remain set in concrete, I would not want the way of assessing risk to be set in concrete. That also has to develop as people's perception and people's understanding of the science develops. Let us take an example: In the early days, for example, and I am sorry to go back, there was a great deal of uncertainty as to why micro-organisms were able to colonise human beings and therefore produce pathological changes. Our understanding of the scientific processes underlying that, has developed by leaps and bounds. That is a very material consideration when you are trying to assess risk. As knowledge accumulates, I am sure regulations have to be developed. At the moment it seems to me—but we are actually, as I stress, at secondhand—we are content.

Lord Walton of Detchant

744. Could I then ask you a question which I have posed to a number of other witnesses? Most of the evidence we have heard has been extremely reassuring relating to potential risks of genetically manipulated organisms and release under present regulations. One person suggested there was at least a remote possibility in the field of, for instance, human health if you were using a viral or bacterial vector in order to carry a gene into human cells, that by cutting out a portion of its own DNA and splicing in the gene product, you would of course have removed potential pathogenicity, but if it was then exposed to a comparable organism of the same species in the wild, then that pathogenicity might be restored. Is this just a theoretical risk, or is it a real one?

(*Sir Mark Richmond*) This is really at the heart of the matter, is it not; because you could write down as it were, sitting in an arm chair, from the point of view of a microbiologist, or biochemist, an entirely plausible way in which that might occur? The question is, what is the probability with which it will occur? That is the thing which is extremely difficult to discover, because each situation is individual. Each case is different and to put a numerical value into the probabilities is extremely hard. Therefore, we have to be cautious.

Chairman

745. I thought you said that you played some part in writing the regulations. Is that right?

(*Sir Mark Richmond*) In drafting this earlier regulation, but that was some years ago.

746. That is true. Can you answer a problem that has been bothering me for a bit during this investigation? Our regulations are based on the EC approach, I gather, and that I am told is somewhat different from the proposals put forward by the OECD some time ago. Can you tell me why the EC was preferred rather than the OECD?

(*Sir Mark Richmond*) I cannot tell you that for sure. I imagine it is connected with our position in the European Community. This area has, as your Lordships will know, very direct implications for the commercial success or otherwise of companies and we are in the European Community.

747. You think it was largely political?

(*Sir Mark Richmond*) Yes, inasmuch as we are in the European Community.

Baroness Platt of Writtle

748. Some of our witnesses have very firmly put that the problem is of lead time in the commercial situation and I was quite interested when you said that the regulatory regime will not unduly prejudice the exploitation of the Science Base by United Kingdom industry, but there have been witnesses who have felt very strongly that because of the enormous number of questions they have to answer and that people may then question the answers to those questions, that they may lose their lead time?

(*Sir Mark Richmond*) Perhaps I might qualify that. That was written from the perspective of the SERC and our involvement at the low risk end. I suppose the other comment I would make is that presumably there is—one should underline *presumably*—a level playing field, in that what is more difficult for our industry would be more difficult for our competitors' industry. I underline the *presumably*.

749. We have heard that the USA regulations are much more "lenient" may not be the word, but more flexible?

(*Sir Mark Richmond*) Yes.

Lord Gregson

750. Is not the importance of the USA regulations a time limit on replies and the fact if you do not reply within three weeks, permission is automatically granted? We heard about some applications held up in the Ministry of Agriculture for at least six months and still had not had a reply. Is there not some problem in that situation?

(*Sir Mark Richmond*) Our experience would be, at our lower level, that that has not been a real problem; but one hears stories of that kind.

Lord Renwick

751. You say you would welcome flexibility in the regulations as they exist. Do you see there is the right mechanism for achieving that flexibility, both for the United Kingdom regulations and as they come from the European regulations or Directives?

(*Sir Mark Richmond*) I do not think that there should be so much flexibility in the regulations as they exist. Where I would like flexibility is in the need periodically to review and to adjust.

752. I understand that. That really is the need for change as—

(*Sir Mark Richmond*) As knowledge increases and experience develops.

753. Do you think there is the right mechanism for achieving those changes? Are there the right mechanisms for achieving that? Are there the right contacts?

(*Sir Mark Richmond*) I think it is reasonable. I suppose the reply might be if the mechanisms are okay for setting up regulations, presumably the mechanisms are okay for reviewing them. I would be reasonably content. There are other issues about the extent to which they do bear in at the top end on the operation of people. I think that area is are more important. I think the mechanisms are there.

Lord Whaddon

754. Sir Mark, you said that over the years public perception has evolved. Has it evolved towards greater acceptance of genetic engineering, or greater reluctance to accept it?

(*Sir Mark Richmond*) My feeling was in the early days—and I really was involved at the very early stages; I went for example as one of the United Kingdom representatives to the famous Asilomar conference where these things were first discussed—there was a great deal of hysteria about. People were pencilling in immensely dramatic scenarios. I think a fair amount of time has passed since then and some of these horror scenarios have not materialised and opinion is becoming more moderate. Having said that, there is experience from other areas which suggest to people that in such areas, like radiation risks and things like that, there are questions which have to be sensibly addressed. Earlier on there was a strong polarization. There was a community that was saying that the world was going to come to an end and another community which was saying: "We are absolutely the best people to decide that. You do not understand, go away and let us get on with it." There has been now, over the years, a coming together of these two communities. The other thing I could say I suppose, is that across Europe, I do perceive very considerable differences in perception, country by country, and as we are now talking about European Community Regulations; that does raise a difficulty. My perception, of Germany and Holland for example, is that people are much more concerned about some of these issues than in other countries. You notice that in other fields too. The one that concerns us in SERC much more, is the risk of nuclear installations, I am astonished by what the population in France will tolerate in that regard. There is no way in the United Kingdom that similar events would pass without comment.

Lord Perry of Walton

755. You say that the public awareness is being addressed actively, through the Joint Advisory Board. Could you tell us what "actively" means and in particular, who is going to finance the activity, because it is a very expensive business?

(*Sir Mark Richmond*) I do not know the answer to that. I do not know if it is proper to say so, but your assessor had a relation to the Biotechnology Joint Advisory Board (BJAB); and I think you will have talked to Dr Dart who is now his successor. Could I suggest you talk to him about that?

Chairman

756. I have always had a fair regard for the French, by the way!

(*Sir Mark Richmond*) Yes, so have I.

757. In your paper, Sir Mark, you quite rightly say your research falls mainly into combined use regulations and then you go on to say that some more work is going on in the field of environmental bioremediation. I would like you to tell me what bioremediation is in the first place and tell me some of the work that is happening.

(*Sir Mark Richmond*) I will probably turn, before long, to Dr Clark, but the bioremediation is an approach that is becoming very interesting to people. It is basically the use of biotechnology procedures in clean-up and areas of that kind. Its falls under another heading, which is sometimes called "clean technology". How do you develop processes and how do you use processes to minimise the impact on the environment; and, if you have had an impact, how do you deal with it using procedures which are themselves benign? One of the problems at the moment is that you can clean up your worse mess. You see it in with oil spills. One of the big areas in biotechnology in the future, very much associated with the chemical industry, is how do you clean things up in a benign way?

(*Dr Clark*) Very quickly to add to that, our interest in much of this has been reasonably recent. We have not been major players in the field. As Sir Mark Richmond said, we have a new programme in clean technology and this particular area has recently launched a new LINK programme in biotreatment of water and soil. Whether we remain players in that after the White Paper is still to be resolved, but the reference to moving into the area referred specifically to clean technology and this new LINK programme.

758. Is this done by developing bacteria or is it chemical or what?

(*Sir Mark Richmond*) There are various ways of doing it. I think the main thrust at the moment, to my understanding, would be that you use biological sources to generate molecules. Some of the clean-up does involve polymers and things like that, which are produced by micro-organisms. The biotechnology comes in where you get those micro-organisms to produce much more of the product.

759. Have any of the companies collaborating in providing funds for biotechnology research within the United Kingdom Science Base, withdrawn their funding or indicated that they might do so, in order to invest in other countries where they think the regime is more favourable?

[Chairman *contd.*]

(*Sir Mark Richmond*) Not to my knowledge in the United Kingdom, but I have heard that companies in Germany, in particular, are thinking of diverting their activities elsewhere. That may be more to do with the perception in those countries, than the regulations. You will have to ask them.

Lord Walton of Detchant

760. I wonder if I might ask a question which is slightly more administrative in its content? There has always been something of a problem in determining where applications for the support of research should be handled at the margins between the responsibilities of the different Research Councils. It is 15 years since I served on the MRC; there were times when it seemed unclear as to whether a particular biological application, should go to SERC or to the MRC for example. Obviously you will have some concerns about the White Paper recommendations about the future of your Council. On the face of it, it sounds a good idea to have biotechnology and biology in a single Council. The question however I would ask you is whether you see the proposals that are now coming forward as being likely, in your opinion, to further the interests of biotechnology as a science, or whether you foresee difficulties?

(*Sir Mark Richmond*) That may provoke a relatively long answer, if you give me a minute or two. I think the first point to make is that there has just recently been published an ABRC review of biotechnology. I imagine your Lordships will have seen that. There is an interesting table in that review which is a matrix of the various areas of science which are relevant to biotechnology and the Research Councils which are engaged in that matrix. You will find in certain boxes, single Research Councils as entries and in others you find two and three. That actually is frequently seen as good news, because it means the people working those areas have a number of funding streams to tap into. I would have thought that overall in the area of biotechnology, this crevice problem (if we can call it that) of applications falling between Research Councils or between funding bodies is not severe; it does exist in other areas, but I do not think it is really grave in the area of biotechnology, because I think the sum of (?) is more than the parts. I think that—to go on to the question of the White Paper—there is something to be said for having a Biotechnology and Biology Council, which as it were would give the subject some real coherence. So I support that. What I think I am very worried about, in the setting up of the new Council, is that areas which are very, very important or will remain very, very important for an engineering and physical sciences Council, namely bioprocessing and certain areas of biotechnology associated with the action of enzymes and things like that (which ultimately is chemistry) will go and, unless we are careful, and unless we are not too restrictive about it, we will open up a gulf between the physical sciences and the biology sciences. I think in this particular area, that would be a move in the wrong direction. I have already, in the lead up to the White Paper, talked to the Chancellor of the Duchy about this and registered my considerable concerns about this gulf that might be generated. I am pleased to say he said that the definitions in the White Paper should not be interpreted too restrictively and I would hope that view prevails. I think it is very, very important. I think if we separate the physics and the fundamental chemistry from the biotechnology, it would be very serious.

Chairman

761. You do see a danger though?

(*Sir Mark Richmond*) I do, I do. I think it is interesting the White Paper is sending signals and I think those signals may to a certain extent run contrary to what I think is best for the subject. It is not accidental, I believe, that the White Paper talks about an Engineering and Physical Sciences Council and a Biotechnology and Biology Council. Technology is put before the science. That is one signal, it seems to me. If by this, a signal is sent that biology and its engineering base is somehow separate from physical sciences and its engineering base, I think, as an extreme, that is nonsense. There has to be some very careful adjustment and my feeling is that the need to send the message that the technology as important, has perhaps overridden what I believe is the importance of keeping the chemistry biology and physics, in close integration, in this area.

Lord Walton of Detchant

762. It is difficult, for example, to see upon which side of the divide biochemistry will sit; how much on one side and how much on the other?

(*Sir Mark Richmond*) I agree and we understand that a group is to be set up now to examine—effectively a Boundary Commission for science—in these areas; and I will be doing my best to make sure that the engineering and physical sciences Research Council has a stake still in some biotechnology, particularly bioprocessing and particularly in molecules of biological origin of interest to the chemical industry; and particularly in the fundamental science on enzymes.

Chairman] I see a further danger which is perhaps to some people trivial, that is the White Paper looked to me to be more like a brochure than a proper White Paper and I have some doubts as to whether or not it will be taken seriously, but this is common place at present and we need not go into that here. I notice the Rhodes Green Paper is blue and has the same defect. I have no further questions. Have my colleagues?

Lord Wade of Chorlton

763. If I could ask Sir Mark, because he has referred on a number of occasions to the perception and importance of the perception, I would be grateful if you could explain how far you think there is a gap between the perception and reality of this science and do you see your organisation having a role, or any organisation having a role to try and explain more clearly to the public, so that perception is a little bit more realistic?

(*Sir Mark Richmond*) The second part first, yes absolutely. I think we have a role, but I suppose one gets into philosophy. You can regard the scientists' view of the situation as a perception and indeed that

[Lord Wade of Chorlton *contd.*]

there is a continuum of perception. This is why it is so difficult to get hold of. What is the truth? One does not know that. Scientists have a view. The general public also has a view. It is a spectrum and I think people like yourself, people who are making regulations, are trying to coalesce this into clear views, clear perceptions; I do not think they are necessarily clear. It is a bit like a pillow, you press it *here*, it comes up *there*. You press it *there*, it comes up *here*.

Chairman

764. I am going to perform a U-turn, having said I had no more questions, I am going to ask one. From your point of view about regulations, Sir Mark, I would imagine you think that there are many other things more important in determining competitiveness, like the patenting system or technology transfer, or the acquisition of venture capital? Would I be right in supposing that?

(*Sir Mark Richmond*) I am sure that is right. I do not believe myself, having talked to people from pharmaceutical industry in particular, that they would not see the recommendations concerned with licensing for therapeutic purposes as being a considerably greater issue than this. Lord Walton can comment on that.

Lord Gregson

765. I wonder if I could change the subject a little? Part of our remit is to look at global competitiveness in this sector. Are you prepared to give an opinion as to whether Research Council support in this area is sufficient to provide a critical mass to support the industrial aspirations that we might have in this sector?

(*Sir Mark Richmond*) You probably are saying, which I think we can all say very easily, that we could do with more money? That is always and obviously the case. I would feel myself, that compared with some other areas where our industrial competitiveness is in question, (I think particularly the physics based industry) there is a much wider range and larger flow of resources available in biotechnology than in work underpinning, for example, superconductivity. The flow from the charities into biotechnology is very considerable. The flow from the charities to the physics based science is negligible.

Lord Gregson

766. Is it a critical mass? There is an entropy of this situation, the amount of industrial activity in this country, in pharmaceuticals etcetera is much larger by the size of the nation and more important in fact to the well-being of the nation than most other countries. It is dominant. What I am saying is, are we supporting the Research Base with a critical mass, relative to that importance in the community?

(*Sir Mark Richmond*) I think the support in that area is better than the support in a number of other areas, which are I think equally important to the country.

Chairman

767. Anything else? In that case, thank you very much. Unless there is something you yourself wish to add, thank you very much for coming.

(*Sir Mark Richmond*) Thank you, my Lord Chairman.

Examination of witnesses

PROFESSOR J E BERINGER, School of Biological Sciences, University of Bristol and Chairman of ACRE and PROFESSOR SIR HANS KORNBERG FRS, Department of Biochemistry, University of Cambridge and Chairman of ACGM, called in and examined.

Chairman

768. Good morning gentlemen. Thank you very much for coming. Would you identify yourselves and tell us something about your approach to this matter?

(*Professor Sir Hans Kornberg*) Thank you, Chairman. My name is Hans Kornberg, as you can see, and my role here is primarily as a practising genetic manipulator, or modifier and secondly, as Chairman of the Advisory Committee on Genetic Modification. This used, in the old days, to have a sub-committee which concerned itself with the release of organisms into the environment. The primary responsibility of the Committee on Genetic Modification is to the Health and Safety Executive, and the Health and Safety Commission, to ensure that the work that is being done, is done safely, that the worker who is engaged in it is not exposed to hazard, that the people he comes into contact with are not exposed to hazard and that as far as practical, the material is maintained in a contained environment. The sub-committee on releases took obvious note of the fact that one of the main purposes of applying genetically modified organisms to agriculture, for example, is to release them into the environment and this has been recognised as being of increasing importance, so the sub-committee, which is under the chairmanship of Professor Beringer, who is on my right, is now an independent (although linked) organisation responsible primarily to the Secretary of State for the Environment, but with cross membership with my Committee.

(*Professor Beringer*) Sir Hans has done an excellent job of introducing me. I am John Beringer, from the University of Bristol. My role is as Chairman of the Advisory Committee on Releases to the Environment. My background is as a microbiologist and microbialgeneticist.

769. I will ask Professor Kornberg one or two questions first and then we will turn to Professor Beringer and turn to you both in consort. Professor Kornberg, what do you see as the main problems in

[Chairman *contd.*]

the contained use regulations? Do you see them changing for the better or for the worse in the future and would you encourage these to become more product specific?

(*Professor Sir Hans Kornberg*) Perhaps I might be permitted a little disquisition on the history of the system. Please stop me if what I say is dreadfully familiar to you. As you know, there has always been an attempt to improve the materials with which society deals. The horse that we see now is a very far cry from the original horse that roamed the prairies and the steppes. Cows, sheep, potatoes, tomatoes, broccoli, cauliflowers, all these things are vastly different from their ancestors, because the processes of plant breeding, animal breeding, genetic exchange by traditional methods, have been applied over centuries. This is a little bit like deciding that say, if I may use a loose analogy, that if you are a Customs Officer, that you will admit only lorries with a yellow number plate. You will select those traits which are desirable. The techniques of which we are now talking, of genetic modification, arose from the recognition that the genetic code is the same for all living organisms and where there are subtle differences—these are differences in regional accents, not in basic language—and that the technology arose particularly in the early 1970s, which would enable us to snip out little bits of genetic material from one organism, snip out a similar gap from another organism and just exchange the two, or insert a gene from one to another. This, of course, entirely novel kind of procedure, enabled not only material to be transferred with great specificity, but it enabled one to construct organisms which had a genetic make-up very different from any that had been previously encountered. It was that that caused anxiety and it was the nature and the realisation of the possible hazards associated with this which led, initially, the scientific community to ask for a moratorium to be imposed, so that no experiments could be done until the questions could be answered: How would we assess the risks of this procedure? How would we put those tests actually into practice and how would we assess the safety or otherwise of this procedure? I was written to in 1974 by Professor Berg, who was one of the people who called initially for the moratorium and was asked to alert the scientific community and the public here in this country, to this new technology and the possible hazards associated with it. I was fortunate, because this was at a time when Sir George Godber had just called hearings on the use of dangerous pathogens and regulations that should apply to them and I was asked to give evidence. This then led to the establishment of a Working Party under the late Lord Ashby and this in turn led up to a series of Committees being established, the first one called the Genetic Manipulations Advisory Group, which then grew into the ACGM, which is the Committee on which I now serve. As a result of these enquiries, a series of regulations were put into place which were however essentially horizontal. In other words, they said it is the technique of genetic modification which is inherently hazardous and it is therefore organisms which have been modified in this way that should be particularly looked at. Much of the regulations that apply to the practice of genetic engineering (loosely called in this country and in the European Community) is based on that concept. Experience has shown over the last, I suppose nearly 20 years now, that the hazards which were estimated to be associated with this technique, or with the organisms that resulted from it, were conjectural. There is no evidence that the technique itself is hazardous and indeed a Committee under the aegis of the OECD and a Committee under the aegis of the US National Academy of Sciences, said that the hazards of genetic manipulation by this means, or genetic manipulation by the traditional means of plant or animal breeding, were really no different and if there were hazards, the hazards would be associated with the product that was formed. It has been very difficult to convey to the public, which has rightly been alarmed about this horrible new possibility, that really the process is very similar to getting coal from a delivery of coal, into your coal shed. You either use a shovel, which means you can very efficiently transfer the coal, but you also transfer pebbles and bus tickets and cigarette ends and anything else that happens to be there, or you use a pair of tongs, which means you pick up each piece of coal individually and although it is slow and tedious and probably more expensive, at least you know what you are transferring. So the procedure of genetic modification is one where we use tongs and just as in my earlier analogy, although the Customs Officer knows that he is selecting certain traits which he recognises as say yellow number plates, if they come from the Netherlands, he does not know what is in the lorries. He does not know whether there is a trailer. He does not know whether there is mud on the wheels. He does not know what else he is transferring, whereas with the process of genetic modification, at least one has some specificity. So the attitude my Committee has adopted—and here I am reflecting I think the consensus view of my Committee—is yes, it is a novel technique, which clearly has to be regulated in some way. Clearly we have to know who is doing genetic modification by this means, that is statutory notification. We have to have means of inspecting the facilities which are being used. We have to be certain there is a Biological Safety Committee, which is aware of what is going on and can estimate the hazards and we therefore have to be certain that it is done safely and without causing damage to man, or if there is an accidental escape, to the immediate environment. Having said that, we also now recognise that the initial fears were conjectural and probably over estimated and that we should work actively to move from the horizontal to the vertical. Again, if I may use an analogy which I have used before, if I were concerned about the consequences of putting the letter "S" into the word "pet", so as to have it spelled out P-E-S-T, what I would need to find out is whether the P-E-S-T is indeed pestilential, what its hazards are and how it should be treated. I would not really be worried as the whether the "S" was transferred there by a typewriter or a word processor or any other technique. It is not the technique we are concerned about, but the hazard of the organism and although I hasten to say, and I am very good at delegating or passing the buck to my friend John Beringer, my Committee has nothing whatsoever to do with product regulations, never-the-less the feeling in my Committee is that yes, we

[Chairman *contd.*]

should go very much more towards a horizontal approach in the European Community, because we feel that is the only way in which we can help the progress of biotechnology.

770. Do you mean horizontal?

(*Professor Sir Hans Kornberg*) I am sorry, I mean vertical!

771. I had a feeling you were inclining towards the vertical!

(*Professor Sir Hans Kornberg*) Lord Gregson knows I have great difficulty in telling right from wrong, never mind right from left.

Baroness Platt of Writtle] My Lord Chairman, could I congratulate the witness on explaining so beautifully? I do not know if he talks to all sorts of children in schools, because it was so wonderful.

Lord Whaddon

772. Sir Hans, from my very limited knowledge, I cannot visualise any circumstances where genetic engineering can achieve a genetic transfer which is impossible by natural or traditional selective breeding methods. Are there, to your knowledge, any conceivable transfers of genetic material possible by genetic engineering, which are not otherwise achievable?

(*Professor Sir Hans Kornberg*) Somebody very wisely said that if an elderly scientists tells you that something is possible, he is probably right. If he tells you it is impossible, he is almost certainly wrong. With that proviso, I would say that the chances of certain types of genetic exchange occurring with great frequency of course depends on the proximity of the organisms to each other and particularly how far the words which are encoded—the genetic material of one organism—correspond to the words on another organism, so that you have the possibility of cross-over occurring and that this happens very easily. I mean dogs get puppies and cats have kittens. It is very rare that dogs have kittens or cats have puppies, because of this contiguity. What we are now seeing however, is a technique which very readily enables us to introduce a human gene into a bacterium and a bacterium to express that human gene in order to make human insulin, for example: it is a very good way of making insulin. What is almost certain is that certain types of crosses—across species barriers—occur much more frequently than we had thought. Every time we look at a crown gall, for example, we know that this is a result of a bacterium injecting its bacterial DNA into the plant cell and becoming incorporated into the plant cell. Professor Beringer being a Professor of Botany, I am hesitant to go any further than that. Similarly, it is almost certain, since we know viruses cause diseases, to do so by integrating their material into the human cell and then becoming released again. It is almost certain that species barriers would have been crossed in this way; but the fact that there are species, means that the frequency of it occurring naturally is rather low and the further these species are away from each other, the less is the frequency. The point is that at the DNA level, a lion and a dandelion are similar, but if you meet them in the field, you notice their difference!

Lord Perry of Walton

773. Can I ask whether you think that the move towards practical regulation of the contained type of product, could be achieved by a British interpretation of the existing EC rules, or whether you think there will have to be a modification to the EC regulations?

(*Professor Sir Hans Kornberg*) I think somebody once said to Carlyle, a lady said to him: "Mr Carlyle, after great thought I have decided to accept the universe" and Mr Carlyle said: "Madam, I think you'd better." The same is our attitude to the EEC Regulations. The EEC Regulations were framed by consensus views being put in by many, many countries and we of course played our part in this. The ACGM was consulted on many points, helped in writing them and our representatives in Brussels put in their bit to try and achieve what is the present regulation, or set of regulations and there are two of course. One is on contained use. The other is on release. The chances of modifying these will depend very much on the willingness of our partners in the European Community also wishing to modify them. I think it is clear to me now and Dr Richards will confirm that, that there are many people in Europe who now feel that they have shot themselves in the foot by being too strict in the regulations. The fact that most biotechnology developments in Germany are now located in France, Japan or the United States, I think will convince them that maybe green is not always the best colour to use when you plan to go ahead. It is all right at the traffic lights, but not otherwise. So my feeling is that yes, we will continue to work for a relaxation and I hope we will and as long as I am associated with the Committee I shall certainly do so, but my ability to effect a change will depend very much on the willingness of others to recognise the fact that there are two points of view, there is a wrong view and there is mine!

774. How far do you think, without modification, can the interpretation of the existing regulations be made to ease the life of the producer?

(*Professor Sir Hans Kornberg*) I think we have been very fortunate in the advice that we have received from our officials—and some of them are behind me—who have interpreted them in a very flexible way. I think that they know enough about the subject and about both the scientific base, the technological imperative and the legal constraints to be as flexible as they permit. I have no complaints on that score.

Lord Walton of Detchant

775. We have been told by some of our witnesses, that the advice given to the European Commission in relation to the Directives to which you have referred, by scientists from across Europe, was subsequently modified by the influence of the Council of Ministers and the European Parliament under pressure from the environmental lobbies, so-called. Is this something of which you are aware and is it a prospect that might make it difficult to modify the regulations in the future?

(*Professor Sir Hans Kornberg*) I have no direct experience of this, but I certainly have heard the same

[Lord Walton of Detchant *contd.*]

story. The answer is yes. It is to me remarkable that the initial hysteria which afflicted the United States in the early seventies on the introduction of the whole concept of genetic manipulation and which led to public hearings in Cambridge Massachusetts—I happened to be there at the time—which led to people tearing up little plots of strawberry plants, because they thought it was going to change the universe and all sorts of things. This all died down and there has been a gradual realisation, which has led to, at the latest estimate, over a thousand biotechnology companies being established, well over a thousand releases of genetically modified organisms into the environment under controlled conditions and a much more sane and relaxed view as to what is the likely hazard. What I find depressing is that ten years later, almost exactly, the same hysteria afflicted Germany and only two or three years ago, afflicted Switzerland. One does not know why one is so reluctant to learn from experience.

Chairman

776. I wonder if we could interrupt you at this point, Professor. Do you think that the Royal Commission here was slightly hysterical too?

(*Professor Sir Hans Kornberg*) As a former Chairman of the Royal Commission, I would never assume the Royal Commission could be other than balanced, sane and judicious in its utterances. I must say that I felt that—

777. I do not think you were Chairman at that time?

(*Professor Sir Hans Kornberg*) No, I was not. I was very much a "Has Been" at that point, but I think perhaps the experience of some members of the very real hazards associated with accidents in the chemical industry, for example, led them to fear that similar things might apply if the genetic technology were not strictly controlled. Of course the Royal Commission's approach is very much a technology one and very much a horizontal one and it was not a vertical one. Although it benefitted from distinguished scientific advice, such as Professor Beringer on my right, it did not entirely accept the scientific view, at least not the biological scientists' view. I would have thought—I am guessing—that if the Royal Commission were to have another go at writing the report, it might be a little less restrictive and it might not demand that every instance of genetic modification experimentation should be so strictly controlled as they were suggesting in their report, for example.

778. You mentioned Carlyle earlier on. It brought to my mind the thought that somebody said of Carlyle that it was a good thing he and Mrs Carlyle had got married to each other, because in that way there would only be two people unhappy, instead of four. He may not be the best witness! I wonder if we could give Professor Beringer a look in for a short time, thank you very much? I would like your views on somewhat similar areas, Professor Beringer. Could you tell us your attitude towards the regulations? Are you a horizontal or a vertical man? How do you think they should go in the future and how does it effect your work?

(*Professor Beringer*) I think from the point of view of releases, it is probably more sensible at the moment to be horizontal than vertical, because I believe strongly that public opinion is something that has not begun to be conquered and I think the main reason for this is that there are virtually no products on the market that ordinary people can see are beneficial and are of value to them, arising from the technology. Until such time as there are, I do not know how the ordinary person is going to be able to come to any decision as to whether they like the technology or not. So in that respect, I am fairly relaxed at the concept that we use genetic manipulation as an indicator for making a risk assessment at this stage. That does not mean that I do not think with particular products as we gain more experience, we should not move to a more vertical way of handling.

779. When do you think these products are going to appear?

(*Professor Beringer*) I think we will see vaccines soon. They are already in the late stages of development. We will see some genetically modified plants, such as cotton resistant to insect attack. We will see some herbicide resistant plants, but they are coming very, very slowly and much more slowly than was originally promised.

780. It might take some time before the public is in any position to make the kind of judgment you are referring to?

(*Professor Beringer*) Yes, because I have to say, thinking on an earlier question of yours to Sir Mark Richmond, I do not actually believe it is feasible to educate the public to accept "the technology" because I do not believe most people want to bother to understand. They want to see something they like and if they like it, technology is acceptable.

Baroness Hilton of Eggardon

781. My Lord Chairman, surely vertical regulation, which actually looked at the risks of the product, would actually go much further towards reassuring the public than horizontal regulation which deals with techniques they do not really understand? People do understand when they see someone has assessed that a tomato is safe, whereas they might not understand the genetic manipulation that has produced it and will always, without a strong scientific background, not understand it?

(*Professor Beringer*) I would agree with you, if we had products at the moment, but we do not at the moment, and I think that is why the existing horizontal basis is a good one from which to work. I have said already that as soon as we start to get the products and we can actually see a sensible area and pesticides is one already in which we are likely to see vertical regulation, then it will make sense.

Lord Wade of Chorlton

782. My Lord Chairman, can I follow up on that, because we had a similar discussion last week when it was then suggested that perhaps some labelling system would enable the public to understand the product was produced from biotechnology techniques and in fact was safe and good and

[Lord Wade of Chorlton *contd.*]

wholesome and everything else? Have you any thought upon the labelling aspects of this issue?

(*Professor Beringer*) As you know already, the Advisory Committee for novel foods and processes is looking into this with the Food Advisory Committee. I think the problem we have with food labelling is the one that occurred with the irradiation of food. No matter what the scientists say, if people have a gut feeling something is intrinsically wrong and it has a label on it, the label actually accentuates that it is wrong. The "E" numbers of food additives are another example where with the best will in the world, trying to give information, trying to make people feel happy by marking something up, it marks up a fear.

783. On the one hand you are saying if we want people's perception to understand biotechnology produced products are as safe as any others, they have to know that they are eating them or using them. On the other hand, you say if we tell them how they are made, they are not going to buy them in the first place? How do you fill the gap?

(*Professor Beringer*) I do not fill the gap. I believe that people, if they want something, are not unduly worried about safety. You can see this with motorcars. Motorcars are sold on the basis of speed and acceleration, both of which can lead to increased accidents.

784. There were no regulations when they invented motorcars.

(*Professor Beringer*) Whether there were regulations or not, the point I am making is if people feel they want something because they see it as desirable, they do not worry over much about the safety and therefore the aspect of regulation is less important to them. How many people buy cars asking: "What is the regulatory basis for this?"

Lord Walton of Detchant

785. But there is a strong lobby favouring the purchase of organic foodstuffs for example. Is it not likely that the same people who go for organically produced food without artificial fertilizers, will also wish to have foodstuffs which are not produced by genetic manipulation?

(*Professor Beringer*) I think there is a very good reason to believe that is true and this is why I say it is terribly important for the industry to come forward with things that people want. That lobby would be impressed and like foods that did not have damage from the insects that at the moment damage that food and if that can be achieved without the fear of something untoward being eaten as well, that will become acceptable even to that group, I am sure.

(*Professor Sir Hans Kornberg*) May I just add one thing, in a purely personal capacity? Professor Beringer referred to products that have developed resistance to attack by pests of one kind or another. In the late 1970s in a school in Lewisham, some 80 school children had to be treated. Some had to be hospitalised, because they ate potatoes which had been bred for disease resistance. What had not been realised by the plant breeders was that the basis of defending the potato against attack, was that the content of an alkaloid called solanine was raised inside the potato, so that the pest would find it extremely distasteful. What they had not realised was that the schoolboy would also find it distasteful and in fact it was quite harmful. There was no regulation, as far as I know, which demands that genetically manipulated in our sense, but nevertheless classically bred potatoes, should be subjected to any kind of control whatsoever. So I would suggest that if Lord Wade's suggestion is followed through and one has a labelling procedure, that one also should demand that potatoes bred by ordinary means should be perhaps supplied with a label saying: "This has been selected by processes which are known to be harmful in one case, but we hope no harm will come to you on this occasion." As regards the other point, I cannot help but remind you of an instance which happened in the early days of the War, some of you will remember that we used to have salmon on points and there was salmon Grade I which was astronomically expensive and nobody could afford the points for that, or Grade II or III. Grade III was affordable, because it was dogfish and it was grey and horrible and nobody would touch it, until one manufacturer came up with a brilliant idea of sticking a label on it saying: "Guaranteed not to turn pink in the can." A similar argument could be applied.

Baroness Platt of Writtle] The real problem though, my Lord Chairman, is this question of the public understanding and the words that are used. Quite a number of words have been used this morning, "genetic manipulation, genetic modification, engineering". These arouse suspicions in the average public mind and they do not know what it means and DNA itself is sufficiently new for most people not to be able to understand it. It seems to me that it is a spectrum and how wide is the spectrum and how are you going to get over to the public the fact that it is not dangerous, when it is not until it has happened for several years that we shall know for certain what the risks are or know more nearly what the risks are?

Chairman

786. Talking about risk, we will maybe have to just wait and see. I am wondering, Professor Beringer, how does ACRE assess the risks associated with the release of a GMO?

(*Professor Beringer*) I will not keep you all day. I will be very, very brief. Primarily we are interested in whether or not the organism itself, or the genes within it, if they are transferred on to something else, might give rise to some harm to the environment. So one of the first things we want to do is look at the parent organism. What is it like? What do we know about it and then look at the genes that have been added to it, or the manipulation to its existing genes and try then to think how might that effect the organisms to alter what it already does in the environment? So if you are looking at a potato plant and you add an insect resistance to it, firstly we look at the potato and ask what its risks are in the environment. We would then ask about the added resistance to insects, how might that make it more of an environmental problem? In doing that, one has to have an understanding of what the genetic manipulation is, though it is very hard for me ever to

[Chairman *contd.*]

understand how that tells you an environmental answer in terms of whether something becomes a weed or whether it persists or whatever; but that is a component of the assessment. Primarily the assessment is on the basis of, what do we already know? What do we know about what has been done and can we put those two together? The difficulty here is with well established organisms such as crop plants, it is fairly easy to say what the weedy potential is of a potato, because we have long experience. The difficulty from a regulatory point of view, is the organisms that are very novel; new micro-organisms may be used for bioremediation, which do not have a history of safe use. As a Committee it would be very hard for us to say: "How safe is the parent? We have modified the parent." You know, we are modifying an unknown into an unknown virtually and this is where the whole risk assessment becomes extremely difficult.

Lord Perry of Walton

787. I am getting a little muddled about what stage we are really at, because Professor Kornberg said there were over a thousand cases of release in the United States. How many have we got in this country? You said, on the other hand, there are not yet any products. What is the difference of time scale from the release of a new potato that is hopefully going to be resistant to a pest, and in marketing it?

(*Professor Beringer*) The time scale is the normal breeding programme of that organism. If you are looking at potatoes, once you have established that the new potato has commercial potential, you then must multiply up tubers, which will take a number of years. In terms of how many releases there have been in the United Kingdom, I cannot honestly remember. It must be in the region of about 40, but they are all developmental. The reason they have been accepted is that they are well established organisms and they are very trivial modifications.

Chairman

788. Have you turned any applications down?

(*Professor Beringer*) We have turned no applications down in the whole history of regulating releases. There have been two proposals for which there was insufficient information. On requesting further information, they did not come back to it.

789. Let me ask you something further about your Committee. Do you find the present system, where there is a large number of questions to be answered, a helpful system, or would you like to see that changed in some way?

(*Professor Beringer*) Well, it is being changed. I think there are too many questions, but that is the first round of regulation. That is the first information from the Directive that had to be interpreted into national law. We are making changes. As you know, we have simplified procedures. That is a process that was driven very strongly from the United Kingdom. What "simplified procedures" basically means is two important things: One, that we can handle the application by postal circulation, which reduces costs and can reduce time. The other aspect of simplification is that it is possible for an applicant to refer to previous information. At the extreme, you could basically say: "This has been done before", refer to a previous application, say what it is you are doing and that is your application. So that enormously foreshortens the work needed and it ought to be better recognised.

790. This is what people mean generally when they talk to us about streamlining?

(*Professor Beringer*) I have no idea what people mean when they talk to you about streamlining. That is what it should mean.

Lord Walton of Detchant

791. I wonder if I might ask a question, which is perhaps more relevant to the work of Sir Hans' Committee and you may say it is outside your terms of reference, but it is one upon which you may have a view. It relates to the field of human health, where through the Hugo project, hardly a week goes by without the discovery localisation of a new gene and its characterisation, often quickly followed by the discovery of a gene product that may be missing in inherited disease. This is bringing us closer to prospects of gene therapy, already becoming a reality in some disease. In certain areas too, the discovery of a gene product has meant that you can make a monoclonal antibody against it and use that for diagnostic purposes. A number of these are being patented. A number of doctors, in particular, have expressed concern about whether it is right to patent human genes, which might subsequently be used in gene therapy in human subjects. I just wondered whether this is an ethical issue which your Committee has considered or whether it is one upon which you have a view?

(*Professor Sir Hans Kornberg*) It is not an issue which falls within the remit of my Committee but I certainly do have a view. I do not think it is an ethical issue primarily; it is a commercial issue, but I think it is also one to which a number of organisations have already addressed themselves, in particular the International Union of Biochemistry on Molecular Biology, of which I am President, has considered the matter and certainly without any qualm agreed that this is a most reprehensible procedure, that patenting should not be permitted, that these should be freely available to anyone who wishes to use them and that any attempt to be forced along this route—and I am afraid that even our Authorities are to some extent being forced along this route—should be strongly resisted.

Chairman

792. I think we regard the questions from now on as being open house, so to speak. It has been suggested to us that if GMOs are assessed for risk under the existing legislation, applications would still have to be referred to your Committee, because there are not enough experts in this field to go round. Is that true?

(*Professor Beringer*) I think from the point of view of environmental releases, there is a shortage of people one can easily chose to make up a Committee, but I would not say the shortage is such it would not be possible to have a number of parallel Committees.

[Chairman *contd.*]

I do not honestly see that a number of parallel Committees is very sensible in terms of cost, or of the efficacy of doing the job, unless one has a enormously large number of applications that one Committee could not handle.

793. I think Professor Beringer, you remarked that some proposals put forward were for trivial changes. Has this led you in any way to apply the considerations of what is known as the "fourth hurdle"? That is, to think of *need* for a product as one of the characteristics that is to be taken into account?

(*Professor Beringer*) I am on record as thinking that the fourth hurdle is a disaster and would lead to East European style industry and development. Fortunately in the Advisory Committee on Releases to the Environment, we are not involved with ethical considerations or considerations of whether or not society *needs* something. We are concerned as to whether or not something will give rise to damage to the environment and I believe that is how it should stay.

(*Professor Sir Hans Kornberg*) Of course in the ACGM we are concerned with contained use and contained use is what characterises industrial production and we have had just an off-the-top discussion on this matter and we echoed Professor Beringer's view and we think that the fourth hurdle is not only unnecessary, but it will be a total handicap and as somebody once said, when asked what use a basic discovery would be, he said: "Madam, what use is a new born baby?" It depends entirely what it grows into and who can predict that something that is cosmetic or unnecessary now, may not be essential some time in the future?

794. I often wondered what the other three hurdles were. I have been told, but cannot remember. To what extent have your Committees been involved in setting up the regulations and to what extent are you now involved in attempting to revise them?

(*Professor Sir Hans Kornberg*) I have already given, my Lord Chairman, a brief account of the fact that the original framing of the regulations and certainly the framing of the guidelines which apply to the practice of technology in this country, were very much in the hands of my predecessors and my own Committee and that we had our input into the European Regulations' framing of Directives. I think that in the future my Committee will very much concern itself with attempts to see how things are working out and we cannot suggest changes until we see how they have worked out in practice and then on the basis of our experience, try to persuade our colleagues in the European Community to adapt and gradually to change the direction in which these regulations go. I do not think we can go further than that at this stage.

(*Professor Beringer*) From the point of view of my Committee, we have been very, very much involved in the regulations, the guidelines that go with them, in the two rounds of public consultation. We were given all the responses. I was asked to chair a small group to look through those and try and draw together recommendations for the Department of the Environment. In the day-to-day running of regulations, at every meeting we have discussion about what is going on and, what the Competent Authorities are doing. We are able to make recommendations to our secretariat. They are asked for advice. At all times I feel there is complete openness in discussion as to how we might move things forward, but understanding of course that we might want to move faster than reality will allow, because it is not easy to change even annexes to Directives unless you have very good grounds for doing so and a desire to do so in itself is not sufficient grounds.

795. Is your input direct to the EC, or is it through Government Departments here?

(*Professor Beringer*) Our input is through our secretariat, which is part of the United Kingdom Competent Authority, which has a direct link.

Baroness Platt of Writtle

796. Is that rather inferring, my Lord Chairman, that Europe is too bureaucratic and that is why it is difficult to change, or is it difficult to change because of the expression of opinion of Parliament, say?

(*Professor Beringer*) It would be a brave person who would say that Europe was not bureaucratic, and foolish as well. What I was trying to say was, we have already made one or two minor changes in terms of simplified procedures, which was not initially perceived as happening as quickly, or indeed *perceived* probably, but I do not think it is reasonable to say, "We want to change this", without a basis of knowledge and experience and in this whole area I think it is experience that is going to be the primary driving force.

797. You said it was difficult to change annexes, where you have that kind of experience—

(*Professor Beringer*) No, I am saying it is *unless* you have that kind of experience, because you do not have a strong ground from which to work.

798. If you have had that kind of experience, then you find you can change?

(*Professor Beringer*) That has been our experience to date, yes.

Chairman

799. As you know, the EC Directives are based on one set of assumptions, which are not quite the same as the proposals put forward by the OECD some years ago. Would you like to comment on that?

(*Professor Beringer*) Yes. I think the advantage of the OECD Group was they could largely say what they would like to happen, because they would like harmonisation, whereas the EC, for all its faults, has to represent opinion from all the Member States and opinion is extremely varied, as has already been said. So I think what we have is the reality on the ground as to what was thought to be acceptable and manageable at the time, which is what we now have as regulations, which was different because the basic concept in developing the regulations was of a different basis. That does not mean it cannot change, but it was just the two points from which people made their observations were different.

Lord Gregson

800. Can I ask Professor Beringer on the regulations, is there unnecessary delay in awarding approvals in this country?

(*Professor Beringer*) As far as we are concerned, we are proud to state that our average is 60 days and we have never taken as long as 90 days.

801. You are not the only Body involved?

(*Professor Beringer*) From the point of view of approving releases from environmental safety, we are. What may happen to things that go to us through other methods of risk assessment is nothing to do with us. It is not an issue in relation to genetic manipulation.

Chairman] Have we any further questions?

Lord Perry of Walton

802. I would like to follow up a point. I did ask about the number of releases and the time it took to get product and you answered it. There have been a thousand releases in the United States and I know there is one product, the tomato, that I came across. How many products are there already in the States, roughly?

(*Professor Sir Hans Kornberg*) It would be a pure guess on my part. Many of the releases are releases of the type that Professor Beringer has mentioned, namely field trials of a limited kind of manipulated maize—or modified maize I should say—or rapeseed or something like that, where there is over and over again an attempt to try and assess the consequences of having different genes in a well known plant, in order to see how it works out. I would guess that the number of products on the market is probably vanishingly small. There are products on the market which are the products of industry, that is human insulin or hormones of various kinds, peptides—you know as much as I do about this—but for agricultural products I would guess there is probably none yet on the market, or if there is, it must be on the figures of one hand. Indeed, the big hurdle still is, as Professor Beringer has already indicated, nobody quite knows how to market these products and get them accepted by the public. We already have seen statements in the press in the United States—I saw that last year—of chains of ice cream manufacturers who said they would never use milk which has been genetically modified. There have been restaurants who have said they would never use any plant materials that have been genetically modified. Of course these are gimmicks, but nevertheless they have a great impact.

Lord Whaddon

803. Could I just add, I seem to remember that coca cola make a special flavour using only naturally derived caffeine. That seems exceedingly successful for generations.

(*Professor Sir Hans Kornberg*) It is similar to the Grade III salmon!

Chairman

804. I always thought it was cocaine they used—that is why I drink it!

(*Professor Beringer*) I just wanted to add something in relation to marketed products in the United States and that is, to me, a very great concern to what has happened to the Flaur Savr tomato, where Campbell is on record as saying they are backing off this area, because of public perception. What the truth of this is, we are not sure, but there does appear from reading the literature of people against the technology, that they are using as an excuse now inadequate supervision and risk assessment and so comments that I have heard that we should move very rapidly to vertical assessment, product based assessment and to cut down on the amount of environmental risk assessment, may themselves be self-defeating until such time as these things are publicly dealt with.

805. Professor Beringer, taking up the point Lord Gregson made about delay, it has been hinted to us that sometimes when you have accepted a proposal, delay has none-the-less occurred due to the activities or inactivities of the Ministry of Agriculture. Is there any truth in this?

(*Professor Beringer*) You certainly will not find me defending the Ministry of Agriculture. I do believe they have very serious problems in one or two areas where they are involved in regulating particular products, and delays can take inordinate amounts of time, but that is nothing whatever to do with us, or to do with genetic manipulation reducing the speed of development of products.

806. But it has to do with the Ministry?

(*Professor Beringer*) Yes, certainly not with me.

Chairman] I think in that case, we seem to have run dry, we will call a halt. Thank you both for a very informative and entertaining morning. Thank you very much. If there is anything you wish to add, please let us know.

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HOUSE OF LORDS SESSION 1992-93

MINUTES OF EVIDENCE
TAKEN BEFORE

THE SELECT COMMITTEE ON SCIENCE AND TECHNOLOGY

(SUB-COMMITTEE II REGULATION OF THE UK BIOTECHNOLOGY INDUSTRY AND GLOBAL COMPETITIVENESS)

Thursday 10 June 1993

MEDICAL RESEARCH COUNCIL

Dr D Rees and Dr D Owen

ASSOCIATION OF BRITISH PHARMACEUTICAL INDUSTRY

Dr J Kipling, Dr R Bolton and Mr A Batchelor

CHEMICAL INDUSTRIES ASSOCIATION

Mr R Grainger, Mr M P Jackson and Mrs E S Surkovic

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THURSDAY 10 JUNE 1993

Present:

Hilton of Eggardon, B.	Renwick, L.
Howie of Troon, L. (Chairman)	Soulsby of Swaffham Prior, L.
Perry of Walton, L.	Whaddon, L.

Memorandum by the Medical Research Council is printed separately

Examination of witnesses

Dr D Rees, Secretary and Dr D Owen, Director, Industrial Collaboration and Licensing, the Medical Research Council, called in and examined.

Chairman

807. Good morning, many thanks for coming. We have received your written evidence. I wonder if you would identify yourselves and perhaps give us a short background submission before we proceed to questions?

(*Dr Rees*) Thank you. I am Dai Rees, I am Chief Executive of the Medical Research Council, Secretary is the official job title. My colleague is David Owen who is Director of Industrial Collaboration for the MRC. The points that I would like to make in introduction are that for this particular issue I do not think MRC is in the thick of the controversy because most of the regulatory issues that concern us and those of our industrial collaborators—but you will be talking to others about that—are covered by the contained use legislation which is more straight forward than the deliberate release, although we have expressed a little bit of concern—it is a relatively minor matter—on the increasingly cumbersome nature of the regulations for certain categories of work that might follow from the EC Directive. I think one special feature of our interest is of course genetic work with humans and of increasing importance now is gene therapy and I must say of increasing interest to industry. It is just coming on to the horizon of potential applicability. This does raise regulatory interests and regulatory issues and these will have implications for our industrial competitiveness because as they apply to experimental and developmental work which is necessary before industry can take them up. I think it is important that we have streamlined legislation which does not hold things up. We do have a problem with the speed with which legal and ethical guidelines and regulations are being put in place, especially when we compare ourselves with the United States where lots of activity is going on apparently relatively unimpeded. The problem really is that of getting regulations in place which will allow work to go forward rather than the nature of any regulation that we anticipate. That is all I wish to say.

808. Thank you. In your evidence you tell us that biotechnology would be the basis of extensive future industrial activity. Some of our witnesses agree with that but others, such people as the Green Alliance and Greenpeace, do not think biotechnology is as important as all that. In what way do you think Greenpeace and the Green Alliance are wrong?

(*Dr Rees*) In the general sense, I think if you look at business forecasts which have been made by professional forecasting organisations such as the Frost & Pearson Study on the uses of monoclonal antibodies, lots of people have done studies of this sort which I think quantitatively are in reasonable agreement. I think if you look at the United States in particular there are actually people not just saying that biotechnology has got great scope for commercialisation but putting their money where their mouth is, putting lots of money in, and these include major pharmaceutical companies as well as private investors.

809. Good. We have spoken quite a bit in our investigation about the regulations obviously, I am wondering to what extent the existing regulatory regime affects your own research activities and, if so, in what way? Secondly, do you think that the current regulations are more onerous for you than the 1989 ones were?

(*Dr Rees*) As I said in my introduction, because we are mostly affected by the contained use regulations I do not think we have any particular problem with the 1989 Regulations. The proposals for the new regulations do propose the upgrading of the safety category of certain types of work, in our view unnecessarily, and with that places an obligation on the research workers to give prior notification of more types of work than in the past, to do more paperwork to document the course of the experiment and so on. Looked at from the point of view of the risk to anybody at all, we can see absolutely no justification for this at all. It is a minor irritation but it just seems pointless and a waste.

810. Would you like to see changes in the regulations?

(*Dr Rees*) We would like to see us sticking with the 1989 Regulations.

811. You would like to go back to 1989?

(*Dr Rees*) Yes.

812. You would be happy with that?

(*Dr Rees*) Yes.

813. In paragraph four of your paper in the first line you talk about the most serious safety issues which arise. How serious are these safety issues? You are implying that they are serious to some extent.

(*Dr Rees*) I do not know whether my colleague would like to add something after I have spoken. What we are referring to here are in a way risks which are not peculiar to biotechnology but are general to any therapeutic agent. Any drug is likely to have side effects and you have to balance, as we say in the

[Chairman *contd.*]

second line: "In part these are analogous to concerns about conventional drugs in terms of toxic-side effects" and so on.

814. Yes.

(*Dr Rees*) I think over the years all developed countries have learned to handle that, to develop legislation to handle these things, to deal with problems as they arise, so that there are no special additional issues raise by biotechnology. Do you want to add anything?

(*Dr Owen*) Only to the effect that biotechnology offers the opportunity for very potent effective materials which can provide the therapies which are not available through non-biotechnology opportunities. I think it is a question of applying what I think are the current approaches with conventional drugs as to how with these powerful new agents society makes a proper assessment of the risks and the benefits. We do not see anything particularly different there but the tenor of our reply reflects the fact that we are looking at very, very potent materials not previously available which have the potential to elicit a whole variety of pharmacological and toxicological response.

(*Dr Rees*) We have a Committee on Safety of Medicines and they know how to do their job and they can handle this like other things.

Lord Renwick

815. Dr Rees mentioned earlier in his introduction that in terms of human research the Americans seemed to be less constrained by the regulations.

(*Dr Rees*) Yes.

816. Is it your opinion that being less restrained has any more danger in their regulations, or our regulations would restrain us possibly to the detriment of our competitiveness? Are we being overly cautious?

(*Dr Rees*) I think it is not so much caution as inertia which is our problem. At the moment the experiments on gene therapy are decided through the National Institutes of Health on a case by case basis considering the rights and the needs of the individual on whom the experiment is going to be carried out and the possible benefits that will flow from that against the risks to that individual which are exactly the same principles as we would apply in carrying out a clinical trial, for example. So the principles are already familiar. Our problem, because the American system tends to be characterised by more urgency and in this case verging on impetuosity, if not actually being impetuous, they have not let the unusual features or difficult features or the unfamiliar aspects of this particular application of the general principles slow them down. They have not spent ages walking around the problem saying: "Are we sure there is not anything we have not thought of?", whereas we are still in this country in that phase. The Department of Health has set up the Clothier Committee, it has recommended that somatic gene therapy is okay, it has recommended that a committee be set up analogous to the In Vitro Fertilisation Approving Committee or Use of Foetal Tissue Committee. We have done this sort of thing before, we have got to do it again for gene therapy. The mechanisms are not in place yet and meanwhile, science is moving forward and we are nearly at the point where there are some very important experiments which may have some implications for our competitiveness which will need to be done. We may well find ourselves delayed by six months or a year. I think that is one problem. The other problem I think is that, not having mechanisms in place, the academics who are getting on with this work are not perhaps as compelled as they should be to be warned that when they do these experiments there are these considerations that they will have to comply with. There may be a certain amount of back-tracking forced on them by us not having the system already there. It has not done us any damage yet but I and my colleagues from the MRC are very concerned and believe we cannot afford any more delay at all.

817. Have you made specific recommendations and if so, may I ask to whom?

(*Dr Rees*) The Clothier Committee has made them to the Department of Health. It is clear what needs to be done, it just needs doing.

Baroness Hilton of Eggardon

818. Can I ask whether you think the inertia lies at the level of civil servants or politicians or government advisors from the scientific community? You spoke about inertia and delay.

(*Dr Rees*) I think it just is a bit slow getting to the top of somebody's pile. I would not like to say whose it is.

819. I did not mean an individual, I meant which part of the system? Do you think it is just a British characteristic?

(*Dr Rees*) It is not politicians, it is the administration and bureaucracy.

Lord Perry of Walton

820. How far is the Department of Health constrained by Brussels?

(*Dr Rees*) On this issue not yet. As no doubt you are aware, Lord Perry, there has been a great deal of interest shown in the general area of genetic manipulation by the European Parliament and a great deal of anxiety in Germany with knock-on effects to Brussels and so on. I think it is to be expected that perturbations will begin to emanate from Europe and that is all the more reason for us to have thoroughly analysed the situation and have a firm position which we can then defend. We will have more chance of having Europe following our lead.

Lord Whaddon

821. Is the MRC aware of the slight feeling of unease amongst the public that scientists sometimes get it wrong.

(*Dr Rees*) Yes.

822. Thalidomide, of course, always sticks in people's minds. Maybe the American regulations are a little gung ho because of the enormous financial rewards and perhaps, therefore, our United Kingdom position is not unreasonable.

(*Dr Rees*) We are painfully aware but I think you can still do things fairly quickly without sacrificing

[Lord Whaddon *contd.*]

thoroughness. If the topic of your study is industrial competitiveness then I think it is only right that the implications for industry's success are actually one of the factors put in the balance.

(*Dr Owen*) Could I perhaps add to that. Through this system the Americans have in place, they have actually had a mechanism to stop some trials which have been deemed by the system to be inappropriate. Although there is a sense of getting on with the job and tackling the issues, one should not present that in a manner which suggests that the Americans are not paying considerable attention to the risk benefit relationship. The outcome of their regulatory process has been to stop some of the trials it has been opposed to.

(*Dr Rees*) I think another benefit of the American system as well is that it has raised the profile and broadened public debate so people have got interested and flushed out all of the positions and had a really public discussion instead of keeping it low profile.

Lord Perry of Walton

823. Do I understand correctly that you are saying they are as careful as we are, the basic controls are the same but the bureaucracy that carries them out is much easier in America than it is here?

(*Dr Rees*) I think it is mixed. A very good question. If you are saying would I agree or have no reservations about all the positive decisions that have been made by the American system, I am not and I am not sure that I would. There have been certain experiments that have been approved because patients were terminally ill, for example, so in a sense rather low weighting was given to the interest of the patient himself. I am not sure that we would have taken that sort of decision here.

Chairman

824. You talk about wider debate in the United States.

(*Dr Rees*) Yes.

825. Debate, as you know, is sometimes a two edged sword. Do you think that debate in the United States has increased the accessibility of biotechnology or increased the uneasiness?

(*Dr Rees*) I do not think I can answer that but I think there is no alternative but to carry the public with us and to be open with the public to elicit their views and take them into account. If it means that there are certain things that we cannot get away with which seem to us ridiculous for the time being, then I think in the long run that is probably a good thing because we have more discussion to g though and an education process and so on. I think we have to do that. I think if gene therapy hits the public as a big surprise in another 10 years after a few things have been done, and maybe a few unforeseen and unfortunate events have transpired, then we will be big losers and we will slip even further back in credibility.

826. Could we go back to your paragraph four. In the fourth line from the top you talk of the concern about the possibility of replication and release.

(*Dr Rees*) Yes.

827. Some of our witnesses have suggested that there was not very much danger from this.

(*Dr Rees*) There was not, no.

828. What do you think?

(*Dr Rees*) As I say, deliberate release is not a live issue for the MRC. As a personal opinion I would agree that I think there is not much, I think the risks have been overplayed. Of course, accidental release is an entirely different matter. We do experiments with a genetically modified HIV virus and all sorts of horrible things like that for scientific purposes and we have absolutely no intention of releasing them. The regulations and the practices must exist to make 110 per cent sure we do not accidentally release them. Accidental release is of course a problem but deliberate release is not a live issue for us. My personal view would be that many of the issues surrounding that have been overplayed in terms of risk.

829. What of replication? I imagine that means spontaneous replication, does it?

(*Dr Rees*) Yes. Again, I do not see that that is an enormous cause for concern.

Baroness Hilton of Eggardon

830. The idea of clones is one of the things that captures the public's imagination. There have been various things that have heightened awareness of that concept.

(*Dr Rees*) Yes.

831. Do you feel that you have any responsibility to educate the public?

(*Dr Rees*) Yes, absolutely. There are all sorts of things. If one wanted to go out of one's way in a sort of James Bond villain sort of fashion in order to engineer species of any sort from micro-organisms up to plants, up to animals and whatever, which are malign and harmful one could do it.

832. Yes.

(*Dr Rees*) If the public is concerned that these mad and irresponsible and malign scientists are going to do that then, of course, we could do it if we were so minded but the unfortunate thing is they think that some of us might get to do it. The regulations exist to make sure that even if there was someone then they could not do it.

833. If I can come back to educating the public: do you actually get involved yourselves in that in any way as a research council?

(*Dr Rees*) Yes, very much. We see it as very important to get material about medical research into schools, for example, so we are producing some literature for that purpose. We have a publication called *MRC News* which we send around, including to the House of Commons and the House of Lords, and I hope that some of you have seen it. We have recently revamped it. I hope you like the new *MRC News*. I consider it my job to get as much exposure as I can for me personally and senior colleagues and research workers with the media about medical research and what is going on, what has been achieved and why it is important. Although it is not within the area of your present report, a particular problem into which we have put a lot of effort is

[Baroness Hilton of Eggardon *contd.*]

legitimacy of use of experimental animals for research which is a major concern for us, to get a more effective debate with the public going on which will lead to more understanding of this situation.

Lord Perry of Walton

834. I find myself in total agreement with your paragraph 11.

(*Dr Rees*) Yes.

835. The problem is I am aware that you and quite a lot of other people are putting a lot of effort into school instruction but it has not actually, as you know, achieved an awful lot in terms of animal experimentation as yet.

(*Dr Rees*) No.

836. The question I want to put is do you not think the implication of paragraph 11 is that a great deal more should be done for general public awareness because school awareness takes 20 years before it really comes through and we are going to have to do something before then? Do you not think it is necessary that people should get together with the academics and the scientists and the government and industry and actually do it?

(*Dr Rees*) Yes, I do. I agree. I would like to commend the White Paper which came out just last week or the week before which flags this up as an explicit priority. I think perhaps having the research councils in the Office of Public Service and Science, where public information and openness and Citizens' Charter and all that sort of thing is, that is very apposite from this point of view. So all of us, including the Minister for Science in the White Paper, have impeccable intentions but I do agree with you that we need to come back to this business like gene therapy and we need to get on with it.

837. It does seem to me terribly important, getting on with it, but somebody has to decide who is going to pay for it. I am asking would it not be wise for the scientific community to get together with the Government and approach industry and try and persuade industry to do it as a joint effort?

(*Dr Rees*) Yes. I think there are delicacies. Colleagues from the ABPI will be coming in in a moment, maybe they are here at the moment. I think although we do, as I am sure you know and you may even be a member yourself, Lord Perry, get together in organisations like the Research Defence Society over animal experimentation, there are divergences. I think there are risks to the Medical Research Council in being identified with, let us say, cosmetic testing. It is not absolutely straight forward but with the spirit of your remarks I totally agree. People have been trying. The Royal Society set up a Committee on Public Understanding of Science and Walter Bodmer and others have been working away quite hard. It is not total inertia.

(*Dr Owen*) The conversation has moved on a little bit but I wanted to make one slightly more optimistic note. We talked a little bit about the sense that biotechnology was stronger in the United States. I suspect that has been greatly helped by the quality of articles which have appeared in serious newspapers. If you open the *Wall Street Journal* or the *New York Times* or whatever, you can read very seriously and accurately presented information. Although it is not very striking I think some British broad sheets are beginning to present information on science in a manner which is educational rather than sensational. I know that Dr Rees and a number of my colleagues—I do myself—spend a lot of time helping journalists to get this information. There is a long way to go but I do see that as a chink of light that I hope we would all encourage. The *Daily Telegraph* perhaps particularly has paid a lot of attention to trying to explain to people what gene therapy is about and I hope we can all be encouraged by that.

Lord Perry of Walton] Getting it into the broad sheets does not get to the people who do not know anything about biotechnology. It is the tabloids we should reach.

Lord Soulsby of Swaffham Prior

838. I am smiling ruefully to myself about the laboratory animals. There was a conference in Brighton I have just been at where I was verbally abused if nothing else because of my interest in that. I would like to come back to the North American scene. You say they are much more willing to put their money where biotechnological research is and it seems to me from experience in the States that it is a much easier mechanism of going from the academic research or academic stage to industry, to translate this into active commercialisation of research, whereas in this country although there are mechanisms for doing this it seems they are very slow, people do not understand them and do not even attempt them. My question really is what in your opinion needs to be done in this country to stimulate the academic research worker to get his research into the more near market product type, not to do it but to translate it into venture capital, support and so on?

(*Dr Rees*) We feel very strongly about this and, again, this is the whole thrust of the White Paper and so on. My colleague here has got something amounting to a set piece on this.

839. I was not aware of that.

(*Dr Owen*) My responsibility within the MRC is to try and make what you are describing happen more effectively and more efficiently and I believe, I certainly hope, we are making significant progress towards that. I think one of the things we discovered was that frequently the most important discoveries which are the basis of industrial competitiveness are usually the consequence of somebody conducting studies designed to answer very important scientific questions. Frequently the specific thing which is exploitable and creates industrial competitiveness is something which comes out of that rather than saying: "I will set out to discover X". The X is much more valuable if the X is a complete surprise and unexpected. That is an important element in MRC and we think the most important thing to do there is to be able to recognise this unexpected X, as I call it, as a basis for exploitation. One of the very striking things in this country when you compare it with the United States is the relative number of so-called start-up R&D biotechnology companies. I would hazard a guess that if we looked at what we might expect on a *pro rata* basis we would probably have only 10, or at best 20, per cent of what you might

[Lord Soulsby of Swaffham Prior *contd.*]

expect in Europe as a whole when you compare it with the United States. The situation in the United Kingdom is actually better than in other parts of Europe. There is a tendency for us not to talk as much as we should about those things which we have which are successful. We do have companies like Celltech, we have Dr Richards here from British Biotechnology, Cambridge Antibody Technology, Therexsys, there is actually quite a long list. More of this is actually happening than people are generally aware of but it is nowhere near as much as it should be. We are trying to get to grips with the obstacles. I think some of the obstacles are cultural, some of the obstacles are availability of capital to support this type of activity but that is showing signs of improving slowly. I think the single place where this could be helped most would be if we could get the United Kingdom Stock Exchange to accept some of the systems analogous to the NASDAQ Stock Exchange that exists in the United States. Dr Richards, I am sure, can tell you far more about the details of the different complexities of listing companies. These types of things offer a much more satisfactory return to the sources of capital. They are in themselves accountable to pension funds, etc., whose money they manage and the climate for them over things like so-called exit routes is more attractive in the States. It would not cost this country any money because the NASDAQ market is itself a profit making exercise. If we could establish something like that in this country we would open possibilities for investment. Those are the things we need to do.

840. What are the hindrances for doing that in this country?

(*Dr Owen*) I do not know what more we do as a Medical Research Council. I think the problem has been analysed *ad nauseam* and we all know it is an exit route problem. The Medical Research Council at a recent meeting declared its intention to try and conduct a proper analysis and to enter into dialogue with the Stock Exchange and try and present our sense of why the situation is not as satisfactory in the United Kingdom and what the consequences of that are as it is in the United States. That is an ongoing exercise and I do not think I would be wise to anticipate the outcome.

(*Dr Rees*) Dr Richards and I were at a meeting yesterday which was organised by the British Association in the Guild Hall to talk about rising to the challenge of wealth creation put by the White Paper. It was held in the Guild Hall in the hope that this would be a general debate which involved scientists, industry, universities, the city and so on, but I do not believe anybody actually turned up from the city apart from the one invited speaker.

841. If this had been held in New York or Chicago you would have had 100.

(*Dr Rees*) Or if it had been here on the property market.

Chairman

842. I wonder if I could shift your attention back to your submitted evidence. Your last paragraph, paragraph 12, refers to a number of other items and the one thing that caught my attention was your very last paragraph where you refer to the need for the reform of European patent law and the need to achieve international harmonisation in the patent field. Could you expand on that?

(*Dr Rees*) Yes. This is a point which I will pass over to David in a moment but this is a point which the ABPI made as well in their submission.

(*Dr Owen*) It is a point that was debated at length at the recent ACOST Committee on Medical Research and Health. Patent laws are crucial to a competitive biotechnology and pharmaceutical industry. We live in an environment where the fundamental laws differ in the United States relative to other parts of the world. We would make the judgment that the United States has deliberately created an environment which gives the United States based investors an advantage and has done so quite deliberately and quite purposefully as a political decision. The single most obvious dimension of that relates to the period which is allowed to inventors, that they may successfully file patent applications for any period up to 12 months following their first publication. So nobody else can come in and steal the idea in the interim but the inventor is not obliged to file the patent application before he publishes. When you are conducting work which is making small steady incremental advances the utility of that is often clear and the appropriateness of filing a patent is usually crystal clear and one can control the process and make sure the patent filing precedes publication. When people make very, very fundamental advances the utility is often not obvious immediately and that can often benefit from public debate and discussion. In the United States that would not preclude people from filing a patent and gaining themselves a competitive position. Outside the United States it simply denies you the access to patent rights. If I could give two examples, because discussions with the MRC never exclude reference at some stage to monoclonal antibodies. There was no opportunity for any public discussion of the utility of that invention because the patent had to be filed before there was any discussion or debate. If you look at the other major contribution to the biotechnology industry that took place, it is the gene splicing activity, the so-called Cohen and Boyer patent which came from Stanford University. That is only filed as a patent in the United States of America because the inventors at the time they undertook that fundamental work recognised no industrial application; as a result of outside people talking to them about what an interesting observation they had made and how useful it might be they were able, in fact in the eleventh month, to file a patent application. That has been worth phenomenal sums of money to the United States and its competitiveness. Its analogue in this country has not made that same contribution and various criticisms have been made. The basic fact was the two things were being conducted under completely different sets of circumstances, one sympathetic to inventors and one, I was going to say hostile to inventors, perhaps I should say neutral to inventors but absolutely not sympathetic. It has made a huge difference. If we sustain that we will continue to have these disadvantages. More and more people, as I say, the ACOST report, colleagues from ABPI and others,

[Chairman *contd.*]

are advising how important it is. Government is not yet convinced or impressed. The only argument that they can give back is why should we change? and no good reasons to sustain the *status quo*, which seems to be sad. It is the inertia again which Dr Rees talked about.

Chairman] Thank you very much. We are at the end of our time. Unless my colleagues have any further questions? Thank you very much.

Memorandum by the Association of British Pharmaceutical Industry

is printed separately

Examination of witnesses

Dr J Kipling , Associate Director, Department of Medicine, Science and Technology, ABPI, Dr R Bolton , Regulatory Policy Manager, International Regulatory Department, Zeneca Pharmaceuticals and Member of World-Wide Regulatory Affairs Committee, ABPI, and ↓fi Mr A Batchelor , ff↓fi Environmental Health and Safety Adviser, British Bio-technology Limited and Member of the Environmental Health and Safety Committee, ABPI, called in and examined.⌊

Chairman

843. Good morning, gentlemen. Could you identify yourselves and say a little bit by way of background?

(*Dr Kipling*) Thank you my Lord Chairman for inviting the ABPI to speak to the Select Committee on this important topic. I am the Associate Director of the Department of Medicine, Science and Technology at the ABPI. I am a full-time staff member. The ABPI, The Association of the British Pharmaceutical Industry, represents the majority of the mainstream pharmaceutical companies in the United Kingdom. Our member companies account for probably 95 per cent of the medicines supplied to the NHS. The ABPI represents the views of its members and I am therefore pleased to have with me today several expert members who hopefully will do most of the talking! On my right is Dr Roger Bolton, who is the Regulatory Policy Manager of the International Regulatory Affairs Department of Zeneca Pharmaceuticals. Dr Bolton is a member of the Association's, World-Wide Regulatory Affairs Committee and is one of our experst on products. If members have any particular questions on products, Dr Bolton will be pleased to answer them. On my left is Mr Alan Batchelor, he is an Environmental Health and Safety Consultant to British Bio-technology Limited and a long serving member of the Association's Environmental Health and Safety Committee. He is the expert to whom the Committee may wish to direct questions on health and safety matters. We are very pleased to be here today, but coming to the end of the enquiry we suggest that the views of the pharmaceutical industry have already been well represented by many of our individual member companies who have already given evidence. I am sure however that we might be able to flag up a couple of extra points. We feel this enquiry is very important for a number of reasons. All sectors of biotechnology have been expressing concern for many years over the increasing regulatory constraints being placed on users in Europe. In addition, we are pleased tht the enquiry is looking at global competitiveness. We note that you have received numerous comments on issues other than the GMO regulations which are having an effect on the United Kingdom's success. Issues such as the funding of the science base, patent protection, the financial constraints facing the start-up companies, and the implications of public understanding. As the Association stated in its evidence to the Government's White Paper on Science and Technology, all aspects of Government policy need to be reviewed to ensure that they are not affecting the competitiveness of the United Kingdom industry. Regulatory constraints are certainly one of them. In reference to the two EC Directives that have been the main focus of the enquiry, the pharmaceutical industry's main concerns at the moment are over the implementation of the Contained Use Directive. It is not that we do not have concerns about the Deliberate Release Directive, but at the moment the majority of our companies working in this field are using the Contained Use Directive either in research and development or in production in contained facilities. We have to look to the future and products will be coming which will contain live GMOs and will be affected by the Deliberate Release Directive. Our specific concerns over the Contained Use Directive are quite simply, the cost of compliance, certain confidentiality issues which still remain, and the categorisation of GMOs. We will be pleased to expand on these and any other points.

844. Thank you very much. Your paper has been very informative. One of the things all of the papers have emphasised is the economic importance of biotechnology, looking to the future mainly of course. We can only guess how important it is in that respect. We had a recent report from CEST which suggested that biotechnology would add only 0.15 per cent to United Kingdom annual growth. Firstly, would you agree with that? Secondly, what would you say about that?

(*Dr Kipling*) I am not an economist. I have however read the report from the Centre for Exploitation of Science and Technology and would like to comment on it. First of all, I understand the report was based on 1984 data, on income and outcome generation. It does not cover what are called intangibles, for example, the contribution biotechnology could make to a company screening for pharmataceuticals. I understand it the reported looked specifically at biotechnology production, products *per se*, and the activities of small biotechnology companies. I have to say I think that aspects of the report are very pessimistic and I do not agree with all of its findings. I think there are many reports looking to the importance of biotechnology—we have seen the NEDO Report, there is also an EC Commission Survey taking place in the near future. I think that biotechnology is going to create far more financial wealth in this country than the CEST report alludes to. A lot of the ptential wealth generation is hidden. ABPI member companies want to invest in the United Kingdom partly because of the quality of the biotechnological and biomedical research here. They

[Chairman *contd.*]

will invest their research here and some will choose to manufacture in this country because of the quality of academic research in the United Kingdom. How do we quantify that? How do you quantify what the next 10/20 years are going to bring? In summary, I think that biotechnology will contribute far more than the CEST Report has said. Some however would also argue that 0.15 per cent growth is actually quite sufficient. As I indicated however, I am not an economist.

(*Dr Bolton*) I would add the view that we need to assess, as some people have referred to, the possibility that biotechnology in medicine offers the opportunity for the third therapeutic revolution, the accessibility of medicines that have not existed previously. If there is a global change in that nature, certainly in the medicines area, which is what I am experienced in, we need to at least ensure that we maintain our competitiveness against the rest of the world and do not lose out to a new set of therapeutic horizons that are available to others where as we in the United Kingdom may experience extra constraints.

845. You are pretty confident that the CEST Report is if not out of date then at least pessimistic?

(*Dr Kipling*) Yes.

846. Let us talk about regulations, which have rather dominated our enquiry you will not be surprised to learn. What do you know about the current EC Regulations? How do they come about and to what extent were you involved in the discussions around them, if at all?

(*Dr Kipling*) Lord Chairman, we have to go back into the mists of time to get to the bottom of this matter. The two EC Directives we are discussing at the moment arose originally out of work done by OECD on GILSP guidelines (Good Industrial Large-Scale Practice), international safety guideliens for biotechnology. What is called by users the "Blue Book" was published in the late 1980s putting forward the first international safety guidelines for biotechnology. Shortly after the Commission, I understand it was DGXI, took over this work suggesting that there was a need for directives in this area. A number of proposed guidelines practices were proposed at the time, with DGXI working on the Environmental Release Directive and another part of the Commission—DGIII—looking at the Contained Use Directive. Eventually DGXI took over both Directives. Just before this happened the industry started getting more closely involved and EFPIA, the European Federation of Pharmaceutical Industries Associations, based in Brussels, and of which the ABPI is a member, had a number of meetings with the Commissioners of DGIII and DGXI to discuss these Directives. I was personally involved in a number of these meetings. I have to say most of our views were totally ignored and eventually the Directives were published in their present format and are now being implemented into national law.

847. You say your views were ignored, do you mean they were ignored or do you mean they were countered by other views?

(*Dr Kipling*) If I could give some particular examples which cause us great problems today and one is the 10 litre proposal for Type A work which was put in at the time.

848. We are familiar with it.

(*Dr Kipling*) If I recall correctly the Commissioner reassured the industry that the 10 litre was just an example, and that it will help companies have a feel for the sorts of volumes it was talking about. It was pointed out to the Commission that once such a figure got into a Directive it would need to be implemented. The 10 litres has remained to this day and has caused industry, the United Kingdom authorities and those of Member States great problems in this area. In our discussions witht the Commission we pointed out the difficulties that the classification of organisms would cause industry. The classifications stayed in over the four or five years of lobbying and we still have those today. A lot of our discussions were, I have to say, on whether we needed Directives at all. I have to say we were not very effective in changing the Directives.

849. You mentioned the OECD proposals. I think I am right in saying that the EC Regulations are somewhat different from the assumptions which the OECD had made, is that correct?

(*Dr Kipling*) They took certain aspects of the OECD proposals, but they were not identical. They grew out of some of the OECD's guidelines.

850. You refer to the fact you would have preferred it if it had stuck to the OECD line rather than modified it?

(*Dr Kipling*) There were a lot of good practical common sense in the OECD guidelines. Also, OECD is international. We were concerned that any particular Directive that came out of Europe could have different requirements, from what was operated in Japan or the United States. OECD would apply across all countries and we would have a real level playing field.

851. There are further discussions going on in Europe about modifying the Directives. To what extent are you involved in these and do you think they are proceeding in an appropriate direction?

(*Dr Kipling*) They are now proceeding in an appropriate direction. As the Committee may be aware, the Commission has set up what is called a Biotechnology Co-ordinating Committee under Secretary General Williamson and he has given a clear indication that he is going to review the Directives. ABPI through EFPIA, has submitted a number of proposed technical amendments we would like to see introduced. The problem at the moment is the Commission is unlikely to seek to amend the Directives until they have been implemented in all Member States and have got some practical experience. This has not happened, and quite a few Member States have not got round to implementing them yet, so we cannot really move forward until everybody has implemented them and some real experience. I hope to see some amendments at the EC level on these Directives.

852. I will ask a very naive question: why do they not all implement the regulations at the same time?

(*Dr Kipling*) Again, my colleagues may wish to comment on this. In the United Kingdom in the HSE and DoE, we have experts who understand the the

[Chairman *contd.*]

technology involved in the regulations and are very conscious of the EC legal system. Also I think that United Kingdom civil servants tend to be very keen to get on and do these things. Other countries may not have the technology, they may have no regulatoty expertise in this field. If they have no such investment in teh technology in the country they may not be particularly bothered to get on with it. There are likely to be a number of other reasons why.

853. Some of the countries which do have expertise are a bit slow. Obviously in places like Greece it would not matter so much, but France and Belgium.

(*Dr Kipling*) Things are beginning to move now in these countries. I think we will see the legislation in place in Belgium and France in the near future, if nto already. I think in the next year or two we will see that all Member States will have implemented them. Other countries of course, like Germany, have particular difficult political problems, they have 30 individual political states to address as well as particularly difficult gene laws to deal with.

854. That seems a good idea to me! We will leave that to one side. Do you encourage our Government to delay implementation until the same time as, for example, Belgium who are an obvious competitor?

(*Dr Kipling*) No, we would not do that.

855. Why do you not?

(*Mr Batchelor*) Perhaps if I could comment on that. I do not think HSE generally accept the view that they want to carry out deliberate delaying tactics. They are usually trying to meet the time frame of the Directive. They will say they will go more slowly if by so doing they will get it right rather than just take the Directive and convert it into our legislation, but I do not think on any occasion it has been suggested that they will deliberately delay implementation in order to be in the middle or towards the end of the group of Member States who are supposed to implement national legislation. I do not think I have heard that come up as an issue but it could possibly be one approach.

856. Yes. Why do you not think it would be a good idea?

(*Mr Batchelor*) I think you would probably have to address that to the HSE who are subservient to their masters in Government.

857. Presumably you chivvy them a bit, do you not?

(*Mr Batchelor*) My Lord Chairman, most of our discussions with HSE tend to be related to content rather than [1] timing. I think HSE in general will try and follow the normal approach of implementing legislation coming from Brussels, having agreed to do so in the normal time frame for Directives, unless there are very strong reaons why these should not be implemented.

(*Dr Kipling*) The problem is once the Directives have been formally published the difficulties arise because the United Kingdom tends to fully implement them fairly frequently. It is therefore always important for us to try and make sure we have opportunities for changing proposed Directives at an early stage at EC level. I think that is where the real difficulties arise.

858. If the Directives reduce your competitiveness in relation to other countries I see no reason why you should be over-zealous in bringing them in.

(*Dr Kipling*) That is a question you need to address to our civil servants. We have commented on this in our contribution to the ongoing Deregulation Exercise, and have put some comments in on the GMO side. It is really a question for HSE and DoE to answer.

Lord Whaddon

859. Dr Bolton, you are a member of the Worldwide Regulatory Affairs Committee?

(*Dr Bolton*) Correct.

860. We have heard of research moving from the United Kingdom to Germany or America, are you aware of research moving outside those areas to countries with zero regulations? Secondly, are you aware of any reason why there might be a need for international control or regulation?

(*Dr Bolton*) Perhaps I need to clarify the role of the Worldwide Regulatory affairs Committee of ABPI. As Dr Kipling outlined my interests are principally in product regulation which relates to the approval of medicinal products for placing on the market. I cannot claim to be an expert in occupational health and safety and in envirionmental legislation. That is within the safety, health and environmental area. Perhaps that could have been made clear earlier, I apologise for that. I think probably Jeff and Alan may be in a position to answer.

(*Dr Kipling*) I would like to split the question. If you are asking whether companies would move to areas for their manufacturing where there are no regulations then the answer is no. Our members would seek to operate to the same high standard internationally. Particularly, none of our members would seek to go to countries where there were no regulations for health and safety in force. On the R&D side our member companies have indicated that they would go to countries where the science base was good. I think that is one of the main reaons for moving research to another country. We are seeing that some of our larger companies are looking at countries like Italy where quality of the science base does appear to be going up a bit. I do not think it has anything to do with the lack of regulations there.

Chairman

861. There was a conference in Brussels last week where Commissioner Bangemann, the Vice President of the EC, said that the Commission wanted the Member States to suggest ways of improving or revising the Directives. What are you actually doing about that?

(*Dr Kipling*) Chairman, we have consulted our members widely on this matter, and EFPIA have put through a position paper listing all the different areas where we would like to see changes. That position paper has gone into the Commission and, as I have said before, we are hoping that these comments will be taken up.

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[1] *Note by the witness:* In our experience HSE are kept to a fairly strict timetable by Government in the implementation of legislation.

[Chairman *contd.*]

862. You put them directly to the Commission?

(*Dr Kipling*) We have gone to EFPIA who liaises directly with the Commission. Also, we have talked to the Untied Kingdom authorities putting forward some changes. Of course it is very early days. We have the regulations now, but what we need to see is how they are going to be implemented. I think more views may come up as time goes on and we actually start seeing what the inspectors want to see and how the different administrative processes are actually carried out. At the moment we just have pieces of paper, and what we need to get is some experience on both sides.

Lord Soulsby of Swaffham Prior

863. Could I just ask: do you happen to have a permanent lobbyist in Brussels?

(*Dr Kipling*) Both the ABPI does and EFPIA spent much time talking to the EC Commission. That is one of the main roles of the EFPIA European pharmaceutical trade association, to represent the industry and to lobby as much as we can where it matters.

864. You have people permanently there?

(*Dr Kipling*) The ABPI has consultants in Brussels and Strasbourg to monitor on our behalf what is going on. On particular issues we will lobby on our behalf but lobbying is particularly the role of EFPIA. In this way there is a concerted European pharmaceutical industry view that is going forward.

Chairman

865. Bangemann also said at that conference that the Commission had no intention of imposing the famous fourth hurdle, which we have heard about a number of times. That was fairly welcome news I thought judging by your reaction but there was a certain amount of scepticism among delegates, they had the feeling that whereas the EC might not impose the fourth hurdle various countries in the EC might dream up a variety of health and safety upsurges which would have a somewhat similar effect. Have you any comment on that?

(*Dr Kipling*) Dr Bolton would like to talk in this context.

(*Dr Bolton*) Yes. The fourth hurdle does of course relate to the approval for the placing on the market of a product which in this case would be a product which is a genetically modified organism. That is, at the moment, a fairly rare beast. To the pharmaceutical industry in general it is welcome news that the so-called "fourth hurdle" or "need clause" would not be introduced because medicines' regulation around the world has always been based upon assessment of quality, safety and efficacy alone and indeed that has borne fruit to the extent that sometimes the full impact of therapeutic benefit for a medicine has not been realised until several years after it has been placed on the market. Therefore quality, safety and efficacy protect the patient but whether or not something has a unique blend of properties which make it particularly valuable in therapy can often only emerge in practice. On the product side for GMOs, I think it is important for the Committee to note that as provided for under Directive 90/220 we are pleased to see in the proposals for a Community Regulation (that is one of their regulations as distinct from a Directive), for the future system for medicines' authorisation in Europe, that where the product is itself a genetically modified organism it is intended that the assessment of the product, such as would be required under 90/220, will be placed within the competency of the Medicines Evaluation Agency. Therefore, there will be a single assessment for the placing on the market and there will not be different hurdles, a double hurdle, two separate assessments, one for its environmental implication under 90/220 and the other for its suitability as a medicine. That is an important fact because the critical element in making an overall risk assessment is to assess a product in the context of its intended use and its benefits. The agencies most competent to make that assessment are those concerned with the approval of medicines. Inevitably we expect that they will consult with environmental agencies but it is a single overall hurdle and that is what is important.

(*Dr Kipling*) It is what Commissioner Bangemann refers to as the "one-door one-key" approach.

866. Quite. We had evidence some time ago now from the DoE where Dr Fisk said that there was: "... the very strong view that differentiation between horizontal and vertical regulation is academic if the regulations are risk based..." Quite a number of people, witnesses whose attention I have drawn to this, have disagreed with him, what do you say?

(*Dr Bolton*) I think from the point of view of pharmaceuticals we feel that vertical legislation is most appropriate for the product even though there may be a raft of more general horizontal health and safety legislation beneath it. I know Dr Fisk took the view that it did not matter which type of legislation you have as long as you carried out the risk assessment properly. While one can accept that view in broad terms I think from the point of view of product authorisation then vertical legislation is essential. That certainly would be the view of the ABPI.

(*Dr Kipling*) The vertical legislation would take into account all aspects of the use of the product. There would be a full risk benefit of what the product is going to be used for vertical legislation goes right back into the production of the product, and addresses all aspects relating to its safety, quality and efficacy. The pharmaceutical industry is used to having horizontal and vertical legislation. What we call horizontal legislation includes, in addition to health and safety at work, things like waste incineration, advertising, labelling. Attempts to introduce Eureopan "horizontal" legislation in these areas is going on all the time. On top of this the pharmaceutical industry has product-specific vertical legislation. The main problems arise when you try and impose both at the same time and companies end up having to submit data to duplicate regulatory procedures.

867. It seems to me you both agree and disagree with Dr Fisk but possibly you disagree more than you agree?

(*Dr Kipling*) I think we disagree more than we agree, yes.

[Chairman *contd.*]

(*Dr Bolton*) I think the key, Lord Chairman, is that we would not want to see any duplication of risk assessment. As long as there could be one logical sequence of risk assessment as the product goes through then we would be happy.

Chairman] Have my colleagues got any further questions? No. We will draw to a conclusion there then. Thank you very much for helping us.

Memorandum by the Chemical Industries Association is printed separately

Examination of witnesses

Mr R Grainger, OBE, Director, Product and Regulatory Affairs, Mr M P Jackson, Group Patents and Agreements, The Wellcome Foundation Limited and Member of the CIA Biotechnology Strategy Group, and Mrs E S Surkovic, Executive, Product and Regulatory Affairs and Secretary of the CIA Biotechnology Strategy Group, Chemical Industries Association, called in and examined.

Chairman

868. Thank you very much for coming to see us and giving us your written paper. I wonder if you would identify yourselves for the record and give a short background statement if you feel you need to.

(*Mr Grainger*) Thank you very much, my Lord Chairman. We are very grateful to your Lordships for inviting us, the Chemical Industries Association, to meet with you this morning to supplement the written evidence. Many of our member companies have, as your Lordships know, already given evidence and perhaps all we can do is paint a slightly broader picture on behalf of the industry as a whole. May I first introduce ourselves. I am Ray Grainger, my title is Product and Regulatory Affairs which implies I am the director responsible for safety, health and environment in the Association and also responsible for the chemical industry's Responsible Care Programme. Michael Jackson is sitting on my right; he is Head of Group Patents and Agreements for the Wellcome Foundation and he is a member of our Biotechnology Strategy Group in the Association. I am sure he will be particularly pleased to identify for your Lordships some of the patent and intellectual property difficulties that we foresee and the challenges that we foresee in that area. Finally, Mrs Surkovic, on my left, is a member of my team in the Association and has particular responsibility for overseeing our biotechnology strategy and activities. My Lordships, you will be aware of the United Kingdom chemical industry's importance in the manufacturing scene in the United Kingdom. We are the largest export earner and we are the fourth largest manufacturing operation. In order to retain that position and improve on it, we need to innovate, to produce new products and even more develop new processes which incorporate better or cleaner or safer technologies. Our expenditure on R&D is an impressive six per cent of our sales but, perhaps more significantly, at the present time we are spending about a quarter of our capital expenditure, capital spending programme, on environment, safety and health protection. In that context, Lord Chairman, we are committed to a Responsible Care Programme which requires continuous performance improvement in safety, health and environment. That involves a very solid commitment and a lot of detailed work in both risk assessment and in product stewardship. I think that this is worth stressing because, as we will perhaps be explaining in some of our later comments, we see product stewardship right the way through from the first inception and R&D right through to final waste disposal as being the key to the credibility of our industry as manufacturers of chemical based products. We do not believe we can avoid responsibility just because somebody else has the direct control of the product or the activity at that particular time. More significantly perhaps we see the high added value products sector as being one of greatest growth and in that sector we see biotechnology playing a very significant and major part. From recent questionnaires and recent evidence, we believe that over 30 per cent of our members are currently using modern biotechnology in some way. Although some of that activity is undoubtedly in the development of new products, we believe a considerable and increasing trend is to use biotechnology as a new route to existing products. We see it as a way of improving yields, getting higher purity, reducing energy, and the reduction of environmental discharge and environmental impact. We have recent evidence of a process development where we have an order of magnitude difference between producing a particular product by a conventional route or by a biotechnology route; with a considerable reduction in effluent discharge as well. In the context of one of the questions that you have asked of us and others, Lord Chairman, we are aware of our own limitations in the amount of information we have about the commercial opportunities that exist in our sector. We have, therefore, just recently commissioned a major review of the market opportunities for the chemical and allied industries with particular reference to the process as well as product opportunities. We will willingly make that available to your Lordships when it becomes available to us, which will be sometime in the early summer.

869. The first thing that caught my eye in reading through your paper was a reference to question eight where you say: "It may be of interest that the United Kingdom lost two major contracts to France in this area within the last 12 months, a decision partly based on our regulatory regime." I wonder if you would tell us a bit about that and particularly how important the regulations were in those two episodes.

(*Mr Grainger*) Perhaps I can ask Mrs Surkovic to take that question in order to describe the detailed overall planning within an international organisation, the thought process that it goes into

[Chairman *contd.*]

deciding where to base its new factory. We are also very conscious of the uncertainties that result from some of our regulations and their implementation. Our information suggests that companies are more inclined to go to a country where they know the outcome; they wish to know the regulatory hoops through which they are going to have to jump before making a decision. On the specific questions, I wonder whether Mrs Surkovic could help me.

(*Mrs Surkovic*) The two companies that we mentioned was a major German company and a major Swiss company, both of which you have already taken evidence from. In regard to the German company, they were negotiating to bring a high added value pharmaceutical precursor for manufacture into this country. This was at the time the regulations were going through. The company were sufficiently unsure as to how the regulations would be written at the end of the day and, given their history with German law, they did not want to find themselves in the United Kingdom under effectively similar laws to Germany. They therefore decided to take their work elsewhere. In both cases, in fact, they went to France.

870. Do you think this is because the French regime is more comfortable than the British?

(*Mrs Surkovic*) I am not familiar with the French regime but certainly the amount of work that seems to be going to France at the moment does seem to indicate that it is easier to operate in France although, as I say, I am not familiar with the French regulations.

871. Do you know if there were other factors involved in the decision?

(*Mrs Surkovic*) Yes, I am sure there were, yes. Intellectual property, for example, may have been one of those. Perhaps my colleague, Michael Jackson, could comment on that.

(*Mr Jackson*) I doubt whether in those two examples there would be any intellectual property aspects. The intellectual property laws in France and the United Kingdom are very substantially similar, both under the European Patent Convention. My guess is that the French authorities are a lot more flexible in the way they apply their regulations and their laws and doubtless there were financial aspects where there could well have been differences. I can only speculate on that though.

872. The difference in regulations was part of the problem but you cannot be quite sure how big a part it was?

(*Mr Jackson*) No, I am not sufficiently familiar but I have been present at meetings where an individual representing the British arm of the German company was very strong that the differences were severe and he could not disagree with the investment being made in France.

(*Mr Grainger*) There is a general point, Chairman. The interpretation by the French regulatory authorities in such areas as environmental legislation has tended to be a great deal more flexible than in the United Kingdom. The other aspect, which is certainly true, is that there seems to be less delay in getting the necessary authority for doing things. One of the messages that comes through over and over again in criticisms that we might make of our present legislation are the delays that seem to be a major feature of United Kingdom interpretation and implementation of this legislation compared with some evidence you heard a few moments ago about the situation in the United States. I believe France is generally a more sympathetic place from the point of view of flexibility and absence of delay. That seems to be a general opinion.

873. You say flexibility, it is a word we have heard applied to Belgium, France and the United States. Do you mean there is an element of the blind eye being turned or do you merely mean it is a more relaxed interpretation of the words on the paper?

(*Mr Grainger*) Not specifically in this area, Chairman, but certainly there seems to be a more intuitive risk assessment carried out by French officials than there seems to be in the United Kingdom and certainly more than those in Germany. Intuition and judgment is perhaps not a bad thing to have when you are looking at an application for anything.

874. Napoleon found that on the way to Moscow! Mr Jackson did mention intellectual property in reply to an earlier question, and he probably heard the discussion we had about intellectual property a little earlier this morning. I wonder if you would care to say something about it now? Do you agree that the present regulations in that respect are unsatisfactory and could be changed, modified?

(*Mr Jackson*) I do indeed agree, my Lord, that the present regulations are very unfortunate. They sensibly and reasonably call for full open information to the public, they suggest at an appropriate time, preferably sooner rather than later, they then go on to say that commercial confidentiality should be respected, but the time limits which are applied are totally impossible. One can conceive of an experiment which is worth conducting, that experiment can take anything from minutes or hours to months or even years, only when the results of the experiment are available will one know if there is anything unexpected or surprising in the results, only if it is unexpected can there be anything patentable. It can then take a few hours or a few weeks to prepare the appropriate papers but if the information, the speculative experimental information before the experiment is undertaken is on public record, everything has been published. We are exactly in the situation which the MRC was explaining to your Lordships earlier, how the United Kingdom lost out on monoclonal antibodies. The drafting of the European GMO Directives was dreadful. I think personally it is very unfortunate Mr Bangemann and the Commission are demanding a year's experience of application of the Directives in a dozen countries, each of them in different ways. The baby will have gone out with the bath water by the time the Directives are amended. It is a nonsense.

Lord Perry of Walton

875. Am I not right in thinking that the British regulations, before the EC's came in, were just as restrictive?

[Lord Perry of Walton *contd.*]

(*Mr Jackson*) The initial drafting of them was just as restrictive, my Lord, but we managed to get some adjustments, particularly in the Contained Use Regulation.

876. I am talking about patent law.
(*Mr Jackson*) I do not understand the question, I am sorry.

877. I understood you were talking about the difference between the American patent law and the European patent law.
(*Mr Jackson*) My comments so far were directed purely to the regulations and the European Directives. My Lord Chairman asked me about the regulations. I could go on to express a view on the US/European patent law?

Chairman

878. I think it would probably help Lord Perry if you did.
(*Mr Jackson*) I agree entirely with what Dr Owen said earlier on behalf of the MRC about the advantages of the US law over the European law with one proviso which is relatively small but could be significant. The introduction of a 12 month grace period will undoubtedly lead to instances where there are complications and uncertainties, but whenever one is in a legal, technical area, there are complications and uncertainties and we will have to live with them. It is the reason why many of my industry colleagues are not keen on the grace period but I believe we have to suck it and see.

879. In your paper where you discuss this matter on the last page, question 12, you note that a Directive on the legal protection is actually being discussed. The discussions are obviously aiming at some form of harmonisation. You then go on to say that: "There are fears that, especially in countries where there is no specialist patent court, the law will be applied in widely different ways, which are adverse to the establishment of a Single Market." How do you suggest that difficulty should be overcome?
(*Mr Jackson*) When the Directive was first published in October 1989, my Lord, there was general support for the concept and the proposal. There was some concern about a number of points of detail. Unfortunately, in the last three years, mainly as a result of vociferous, very vocal pressure groups, the points of concern have become even bigger points of concern and the European Parliament in its decisions has moved from the intent of clarifying and unifying the law to having a law which controls industry more. Industry maintains that there are adequate controls in place, if more are needed they should be through the control regulations and not through the patent law, and that the patent law should be clarified. One has to remember that in Europe there is a wide spectrum of cultures and industrial experiences and states, levels. In Germany, up to an extent in France, certainly in Holland, in the United Kingdom, there are well established court precedents on patents. In the other countries there are not and if you go to court—and I have direct experience of being in court in most of the countries—it is a lottery. It is difficult enough in this country, I can assure you it is a lot worse in the Latin countries.

880. Presumably there is a Court of Final Appeal in Luxembourg, does that help in any way?
(*Mr Jackson*) If you have enough time and enough money, but business cannot wait five/ten years and spend £10 million to get there.
Chairman] I had a feeling you might say that!

Lord Soulsby of Swaffham Prior

881. Could I follow up on this question 12. I was most interested in your final hurdle that you have delineated and presumably that is the major hurdle where you say: "The final hurdle which we see to many companies using this technology is one of ignorance." I do not think we have had this put to us. I thought the ignorance was a label to the general public about biotechnology, which we would accept, but I have never been aware the main role where ignorance lies is in relation to business managers, managers of business, that are ignorant of biotechnology. What is being done about that by you and by other organisations to educate the business managers that this is an area of development worthy of being promoted?
(*Mr Grainger*) Perhaps, your Lordship, it is worth saying why we make that comment and make that assertion. As a non-specialist in this area I believe the language that is used is a very difficult language even to someone who is already technically qualified and working in a scientific activity. There are many chemists and physicists in the chemical industry; I suspect that the majority of them are woefully ignorant of biotechnology. There is potential there within the chemical industry, let alone within other industries. We believe that this level of ignorance applies at what we would call the middle management technical level within our industry. We feel this sufficiently strongly to sponsor a major conference with the help of the DTI in October of this year where the intended audience is indeed business managers. If the comments that I made earlier about business opportunities are correct, we are not talking about something that is novel and that is going to be exploited in a new situation; we are asking technical managers to think about the possibilities of this new opportunity, this new science, in the context of things that they are already doing. For example, they might have a 20 stage chemical process; how fascinating it would be and how beneficial to everyone if with some help from biotechnology we could get it down to one or two stages, with energy saving and effluent reduction—and also some very good business opportunities as well. So we are quite convinced that in addressing the overall ignorance of which you spoke we are, at the moment, lacking our own managers as advocates and disciples on this particular subject.

Chairman

882. In question 2 of your paper you refer in the third paragraph there to the environment and you say: "Environmentally, the techniques of biotechnology, in many cases, offer a far superior route to the same product via a more

[Chairman *contd.*]

environmentally benign process...". I wonder if you could explain that to me?

(*Mr Grainger*) We see biotechnology and GMOs as part of a process of improving the techniques of making chemicals; perhaps we could draw an analogy to a catalyst in a conventional chemical process. There is already a lot of evidence that we can get better and more efficient processes, by imaginative use of GMOs and biotechnology techniques. If we take the current programmes of trying to reduce environmental impact and environmental discharges from the chemical industry—which is a very considerable pressure at the present time from Her Majesty's Inspectorate of Pollution—we believe that the use of best available technology, not involving excessive cost, will increasingly involve us in the use of biotechnology techniques.

883. How would that be more environmentally benign?

(*Mr Grainger*) Because we are either reducing the amount of effluent or we are reducing the environmental impact of the discharge. Certainly the example I gave a few moments ago of a 20 stage process coming down to a single stage process would certainly show such benefits.

884. It is fairly obvious there would be an improvement if you reduce the amount of effluent, I can see that well enough, but are you suggesting that the effluent from the techniques of biotechnology are—to use an unscientific word—cleaner than other effluents, is that what you are saying?

(*Mr Grainger*) Not necessarily, Chairman, but they could be. Indeed, in improving your process and improving your yield the probability is that you are reducing the environmental impact. Also, of course, although not strictly an environmental impact, you would probably reduce energy consumption as well.

885. I have one other question. In your reply to question four you say: "There are safety issues which we feel we have successfully addressed..." I wonder if you could say something about that? I would like to hear of successes in this field.

(*Mr Grainger*) Perhaps it is best described in terms of the chemical industry which has been a regulated industry for a long period of time and which has experience in dealing with hazardous situations. Because we are handling so many hazardous products we have had to develop techniques of assessment which take account of exposure and the potential harm caused by that exposure. I would suggest that as an industry, we are more accustomed to coping with hazardous situations, indeed we are often accused of dealing with them all the time. We are developing risk analysis, risk perception techniques for chemicals; are developing those principles in conjunction with HSE and the Department of the Environment for all new and existing substances. These techniques will help us a great deal in doing relevant risk assessments and priority setting and to look at various hazardous activities, including biotechnology. I wonder if Mrs Surkovic could comment on that because it is an interesting example of industry/government collaboration.

(*Mrs Surkovic*) Certainly. As you will no doubt gather we are more experienced with chemical legislation than any other legislative areas. About five years ago, we were approached by the Department of the Environment and advised that there would be a risk assessment requirement for both new and existing chemical legislation. We have spent the last five years working on a series of projects with a number of government departments—the Department of the Environment, HSE (Health and Safety Executive), and the Department of Health and MAFF—to develop a priority setting process for existing chemical regulations and a risk assessment process for both new and existing chemicals. Those have now been completed and we have sent them as a United Kingdom view, from both industry and government, to DGXI in the European Commission. They have been quite successful and are certainly a good example of how industry and government can work together. Just coming back if I might to the Contained Use Directive, I think it is important to point out here a fact that perhaps is overlooked from time to time, that risk is a function of hazard and exposure, and contained use, by its very name, gives rise to very, very little exposure indeed. Therefore, we feel in the Contained Use Directive the risk element has been far, far over-emphasised given that there is very little or no exposure.

886. I take it what you are really telling me is that the chemical industry is extremely experienced in dealing with hazardous matter and in assessing risk and that the well tried methods with normal improvements would be quite capable of dealing with biotechnology as well as any other technology?

(*Mr Grainger*) I think certain minimum standards will have to be set for, the engineering of a biotechnology process and the resulting effluent and anything associated with it. There will have to be certain minimum standards. Once you have established those minimum standards in a process and if it is seen to be necessary to go beyond voluntary risk assessment, you then face the question you asked of ABPI earlier, the relevance of legislation from a vertical Directive related to the product rather than a series of regulations/Directives related to the horizontal aspects of the process.

Chairman] I did not ask you that because I thought I could guess the answer.

Lord Whaddon

887. Thinking of the stupendous sums being spent in America at the moment cleaning up after chemical processes where the risks were not appreciated years ago, does the industry insure against unforeseen risk in biotechnology?

(*Mr Grainger*) There are a number of insurance initiatives going on in this particular area. This is all about gradual pollution with unforeseen future effects. Currently there is a lot of debate about an exclusion clause related to biotechnology and biochemical activity, so I think we have a lot of hard work to do.

(*Mr Jackson*) It is an enormously difficult area, particularly because some of the problems in the USA might have been caused by irresponsibility, others--I am sure—people genuinely believed there

[Lord Whaddon *contd.*]

was no problem at the time when they did it and what they did and it is only over a period of time that the adverse impact has emerged. How one can anticipate what the cost of that will be is very critical before one can say what a reasonable insurance premium will be. I do not know that there is any clear answer but a lot of people are wrestling with it.

(*Mr Grainger*) The risk assessment you need to do for the present situation is not valid for some time in the future. Some of the risk assessments that are carried out on contaminated land and the possibility of clean up tell you that it is better to leave well alone. That that particular type of decision seems to be missing from some of the super-fund thinking in the United States at the moment.

(*Mrs Surkovic*) If I could just add one other point, my Lord Chairman. If an insurance risk was to be worked out from a 'claims made' base on those genetically modified organism released to date it whould be very low, as , I think it is important to note that we have got 20 years of safe use of genetically modified organisms behind us and so far there have been no problems at all.

Chairman

888. Any further questions? I wonder if there is anything you would like to add to what has been said?

(*Mr Grainger*) I think there are three points which we have already made which are worth stressing. The first point definitely relates to the carrying out of proper risk assessments. As people who have had experience in this area we find some of the proposals in the Directives and regulations pretty superficial and not in accordance with what we would believe to be scientific assessment of risk. We, the chemical industry are like the pharmaceutical industry most concerned about the inadequacies of the regulations for contained use where we believe that the point made by Mrs Surkovic about virtually nil exposure or very low levels of exposure has been insufficiently taken into account. The other thing is to say that as a chemical industry with a pretty bad public image in chemicals, we are very well aware of the difficulties that lie ahead in getting public acceptance of our activities. We have been through a lot of this before and we have a number of programmes, for example with the residents people around our factories, with the public at large, with pressure groups and environmental organisations, with schools and universities where we have educational programmes. Indeed, although it is a fairly hard battle, we constantly communicate with the media to try and get a few good messages across amongst all the others.

889. You must have been quite pleased with Martin Lewis when he asked for good news the other day!

(*Mr Grainger*) It is good news that they are thinking about good news, yes.

Chairman] Thank you very much.

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MINUTES OF EVIDENCE
TAKEN BEFORE

THE SELECT COMMITTEE ON SCIENCE AND TECHNOLOGY

(SUB-COMMITTEE II REGULATION OF THE BIOTECHNOLOGY INDUSTRY AND GLOBAL COMPETITIVENESS)

Thursday 24 June 1993

EC COMMISSION

Mr K Mehta and Mr A van der Meer

GREENPEACE

Dr S Mayer

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THURSDAY 24 JUNE 1993

Present:

Gregson, L.	Renwick, L.
Hilton of Eggardon, B.	Soulsby of Swaffham Prior, L.
Howie of Troon, L. (Chairman)	Wade of Chorlton, L.
Perry of Walton, L.	Walton of Detchant, L.

Written Memoranda are printed separately

Examination of witnesses

Mr K Mehta, Head of Biotechnology Unit, and Mr A van der Meer, Biotechnology Co-ordination Committee, EC Commission, called in and examined.

Chairman

890. Mr Mehta, we hear that Mr Garvey of Directorate General XI cannot be present today. If at the end of the evidence here you feel that Mr Garvey can add something we shall be quite happy to receive further comments in writing at a later date. Would you perhaps identify yourselves for the record and tell us something of your position in the hierarchy of the EC?

(*Mr Mehta*) My Lord Chairman, thank you. I am pleased to have this opportunity to give evidence to the Committee on the EC biotechnology policy today. If I may introduce myself, my name is K Mehta and I am head of the division that deals with biotechnology affairs at the directorate general for industry, in particular regulatory questions, policy, competitiveness. Perhaps I may also introduce my colleague, Mr van der Meer, who is secretry of the Commission's Biotechnology Co-ordination Committee. If you will permit, my Lord Chairman, I should also like to reply for Mr Garvey. He requested me to inform your Lordships that in view of the limited notice given in the week leading up to the meeting of the Council of Ministers for the Environment it has not been possible either for him or for those specially charged with the preparation of the directives 90/219 and 90/220 90/219 to attend today. Therefore, my colleague and I will not be in a position to answer all of the questions that the Committee may care to put to us, but the Commission's evidence for the Committee will be completed by written submissions.

891. Good, thank you. Needless to say, a good deal of our discussions have been centred upon or fairly near the two directives to which you have just referred, Mr Mehta. I wonder whether you can tell me where these directives originate?

(*Mr Mehta*) My Lord Chairman, may I make an opening statement?

892. Please do.

(*Mr Mehta*) Your Committee, my Lord Chairman, is engaged in a timely, a thorough and an important enquiry, which the Commission welcomes. As you are aware biotechnology also holds out the promise of the development of a wide variety of beneficial applications in medicine, in pharmaceutical production, in agriculture, in pollution clean up and in many other fields. However, its application raises a number of issues—regulatory, environment, health and consumer choice. The European Community has been involved since the mid 1970s in biotechnology. The policy that has been developed is characterised by partnership between Community institutions, Member States and interested parties from all sides. Community policy started with the adoption of the biomolecular engineering programme, which had a budget of Ecu 15 million between 1982 and 1986 and which funded biotechnology and beyond. Several other initiatives have since been taken not only in the research and development area but also in the regulatory field. The Commission announced its further policy in the 1991 communication on competitiveness for EC bio industries submitted to Council and Parliament. At the present time the European Parliament is also preparing a report on this communication. As far as the Industry Council later on in 1991 is concerned the Council adopted many of the recommendations and the most important of these were that the Commission continue to adopt Community legislation and implement measures as soon as possible, that biotechnology products will have to be regulated under the Community's existing sectoral legislation and the Commission will only do particular regulation where case by case examination indicates that this is necessary. There have been initiatives on standards and there have been initiatives on research and development programmes and in the new framework programme large, substantial reinforcement has taken place. Biotechnology inventions should be given appropriate intellectual property protection and ethical questions should be identified and discussed. The Council then also requested the Commission to prepare a statistical base for biotechnology and to continue the process of monitoring competitiveness of the biotechnology of EC based firms. At the present time what is the state of the Commission to put in place these recommendations? We are far along that line. The main focus for today's discussion is the actions that I have just mentioned. In the recent stock taking note which I believe we have made available to the Committee, my Lord Chairman, you will see that considerable progress has been made in implementation of the directives 90/219 and 90/220. In nine Member States they are already implemented and in all Member States competent authorities are appointed. Recently in respect of medicinal products the Council of Ministers has adopted new product legislation. For novel foods and plant seeds, such legislation is in discussion in the Council and

[Chairman *contd.*]

Parliament or is in preparation. That is my initial statement, my Lord Chairman. Now if you wish I can try to start with the question that you posed to me.

893. I am wondering where the two directives came from and what were the criteria used to draw them up. You will recall that the OECD thought that there was no scientific basis for specific legislation for the implementation of rDNA techniques. I am wondering why that view of the OECD was ignored?

(*Mr Mehta*) My Lord Chairman, in the OECD document if you look at that the recommendations do not say anything about the type of regulations that would be put in place. As to the origin of the directives if you will permit me, my Lord Chairman, I should like to read out how we have seen it. This goes back to the 1975 conference where the regulations of biotechnology were first discussed in a wide public domain. The concerns about rDNA research resulted in the Commission's proposal in 1978 to impose strict containment standards. In 1982 the Council adopted a recommendation, 82/472/EEC, concerning the registration of work involving recombinant DNA. It stated that national authorities should maintain the registration of rDNA work. In its 1983 recommendation the Commission had emphasised the regulatory aspect not only to anticipate commercial innovations from biotechnology but to create harmonised conditions for the common market. In particular the Commission made clear that they would put forward general or specific proposals appropriate to create a regulatory framework suitable for the development of the activities of the bio industries and for the free circulation of goods produced by biotechnology. In that year also the OECD established an expert group focusing on rDNA safety. The work of this group ultimately resulted in the "blue book". On the basis of the work of this group in 1986 there was a Council recommendation concerning safety considerations for the application of recombinant DNA organisms in industry, agriculture and the environment. This, you are quite right, formed a reference point for all OECD countries. It mainly identifies scientific criteria for the safe use of rDNA organisms in industry, agriculture and the environment and equally provides a scientific framework for risk assessment of rDNA aplication. In 1986 the Commission sent a communication to the Council on a Community framework for the regulation of biotechnology, document COM/86/573. On this basis a number of consultations took place with outside experts, scientific and academic. In 1988 the Commission submitted proposals to the Council for three directives, which have become 90/219/EEC, 90/220/EEC and the directive on worker protection. As you know, my Lord Chairman, these were adopted in 1990, nearly two years later. Therefore, the EC biotechnology framework is built up on the precautionary principle as part of the health, safety and environment policy of the Community. It has also been drawn up with the objective of harmonising the laws of Member States in order to permit the proper function of the internal market for biotechnology.

894. That is very interesting, Mr Mehta, and I shall look at it closely later. However, I am not quite sure that it takes me to the point for which I am looking. As I understand it, the OECD thought that there was no scientific basis for specific legislation or regulation. That may or may not have been right, but that is what I think it said. It then set up a number of principles and guidelines. As far as I can make out—and you will correct me if I am wrong—it was the guidelines that the Commission used in getting up its directives rather than the scientific advice?

(*Mr Mehta*) My Lord Chairman, I think if you look at the work in the OECD document in which the Member States and the Commission participated and at the recommendations of the OECD Council which the OECD adopted it does not specify any particular regulations. As you know, my Lord Chairman, the OECD works in a way by consensus and it works in a way to leave the Member State governments to implement in the manner appropriate to their institutional framework and the way in which the laws are set up. I think that you will find that the recommendations were taken on board by all OECD countries, including the Community. As regards the specific question about the scientific basis, if you look at the two directives 90/219/EEC and 90/220/EEC I think as far as scientific aspects are concerned, data requirements, risk assessments and so on, you will find that what exists in the Community under these two directives is very close to and identical with what exists elsewhere and they conform to the OECD guidelines.

895. Nevertheless, Mr Mehta, as I understand it, the Member State experts were dissatisfied with the progress in the drafting of these directives and expressed these views at the time in the late 1980s, I think it must have been. The views of the experts however were swept aside. Now why was that?

(*Mr Mehta*) As I have said, my Lord Chairman, the Commission already in 1988 sent its proposal making its proposition on these directives.

896. Yes, but I am talking about 1987, Mr Mehta?

(*Mr Mehta*) You are right, but in making the proposal the Commission took advice from a wide section of experts, not just from academic and the scientific domain but also industry and other domains and then in the Council itself the directives have to be discussed for adoption and, indeed, in Parliament there was a further opportunity for consultation of experts and communication to the Commission so there was a two year period before the directives were adopted. If you are making the point that there was not adequate consultation, I think that there was, given the time period, a lot of consultation.

Chairman] Well, that may be so.

Lord Perry of Walton

897. Was it not the case that after the consultation the directives then went through to the Commission, then from the Commission and were modified by the Parliament?

(*Mr Mehta*) My Lord Chairman, I think that the procedure is that before the Commission presents its proposal to the Council there is wide consultation. Once it goes into the Council again there is modification that may be incorporated in the Council

[Lord Perry of Walton *contd.*]

and later on in the Parliament. It was in fact the case regarding the discussion in Parliament that the Commission had not taken adequate account of many of the other points that had been made which would have made the directives stricter than they were.

898. Would that not make the directive as it finally appeared quite contrary to what the experts had originally advised?

(*Mr Mehta*) My Lord Chairman, it is a long procedure. The Commission adopts a proposal that incorporates the advice of its own experts, and that of an expert group of Member States. Then there is the discussion in Council and in Parliament and once again you go through the arguments you already had before and the position there and the dispositions of the directives may also change and be modified. If the Commission can accept those modifications it may do so, and that is what it has done in the past.

Chairman

899. One of the problems with regulations of this kind, Mr Mehta—and this is common to all countries—is that there is a scientific approach and a political approach and they do not always coincide. We are wondering if the main impetus for drafting the directives are political rather than scientific. In particular it has been suggested to us from time to time that the influence of green politics in Germany was quite influential in determining the nature of these directives. Do you think that there is any truth in that, Mr Mehta?

(*Mr Mehta*) My Lord Chairman, no, the Commission considers that there is no disproportionate influence of green thinking in the drafting of these directives. In fact, as I said, we were criticised at the time that there had not been more complete consultations of every kind with environmental or other NGO bodies.

900. There is another aspect of drafting of these regulations. As I understand it, Directorate General XI and Directorate General III—and DG III is yours, is it?—were concerned. I am wondering to what extent the lead was taken by DG III and to what extent the lead was taken over by DG XI?

(*Mr Mehta*) My Lord Chairman, in any proposal of the Commission different services, XI, III, VI, in fact all of the services, are consulted. Those who have particular competence have more to say. In this particular case I think both the services had equal influence on the proposal. Finally, it is the proposal of the Commission, the college adoptes it and how each service starts and so on is not an important issue because the college has the opportunity to discuss it before adopting it in the Commission.

901. Was there any different in view and in attitude between DG III, which is industrial, and DG XI, which is environmental? Can you tell me that?

(*Mr Mehta*) I do not think that there was any difference, in fact, my Lord Chairman. If you look at the original proposal of the Commission you will see that this is an important point, that is, what you have said. DG III—internal market and industrial affairs at the time—is responsible primarily for products' first approval on the market. In the original 90/220/EEC proposal of the Commission the directive had a part B referring to research and development, and part C concerning the placing on the market of products containing genetically modified organisms so that you have a regulated product and you have a regulated person. Part B is more to do with before you actually put the product on the market and the deliberate release in the course of that. I think that you will agree, my Lord Chairman, that that is far more an environment aspect. If you look at the original directive and the proposal the Commission put in part C it says that Articles 9 to 16 do not apply, and then there is a list of products for which there is a specific risk assessment, medicinal, food, veterinary products and so on, and any others for which there would be specific risk assessment, just to ensure this one door, one key policy. If you already have certain product regulations and then there are new products under the technology this is not the first time there has been new technology, and even in traditional chemical or other you have new technologies, but the products should go through the same kind of procedure. Therefore, I think that it is a balance between the interests of what you might call putting the product on the market and the environmental aspects. This is to be found in the final directive, part C, which foresees very clearly that where you have a specific risk assessment similar to that which is laid down in the directive 90/220/EEC then those specific articles, that is, Articles 11 to 18, no longer apply. That is what the Commission has proposed and the Council adopted for medicinal products and was adopted last week.

Lord Walton of Detchant

902. In your own submission, Mr Mehta, you say that because of the rapid developments and technical progress in the fast-developing field of biotechnology the full use of the simplification mechanisms foreseen in directive 90/220/EEC on the deliberate release of genetically modified organisms is a priority and that you are preparing in collaboration with Member States proposals for simplified procedures. Does this mean that you now accept that the initial directive was too restrictive and that this process which you discussed is likely to lead to a modification and relaxation of the directive?

(*Mr Mehta*) In the directive, my Lord Chairman, if you look at Article 6(5) it already foresees that on the basis of experience acquired over time a competent authority may introduce a simplified procedure. This simplified procedure, it is clear, would be beyond what is already possible in the directive. The directive foresees in many places options for the competent authorities where they can have what might be called a more flexible procedure. In the United Kingdom you are obviously aware that if you have a deliberate release in many sites the authorisation for that can be given at the same time.

Chairman

903. But then all you are telling us at the moment, Mr Mehta, is that the directive allows the things to be changed in due course. The question was rather, do

[Chairman *contd.*]

you think that it needs to be changed because there were mistakes in it and it was too restrictive?

(*Mr Mehta*) If you are asking for the short answer, my Lord Chairman, I should say no, not because of that reason; I think that the directive foresaw that it would arise and it is because the situation has now arisen, we have the experience, why not use the simplification? Simplification can also involve exchange of information between competent authorities of different Member States. When the directive first came into force it was clear that it was not really possible to simplify. We have now 150 field trials for plants and it is clear that there are opportunities to exploit that experience.

904. In other words, the directives are final but you are going to change them nevertheless?

(*Mr Mehta*) You cannot change the directive, my Lord Chairman, without going through a procedure of Council and Parliament, so a simplified procedure is foreseen for the good reason that in the new technology it is clear that in the beginning without the experience you may want to allow for this opportunity. I can mention here that what was possible for plants in 1986 in the US is totally different from what it is today. Various simplifications have been introduced. It was not because the US policy statement of 1986 was wrong; it was simply that having had six or seven years of experience they were able to see very clearly what the risks are and they have been able to take procedures that are more adapted to a situation where the risk is negligible. Therefore, the simplified procedures would not mean greater risk, and I think that that is a very important point, my Lord Chairman.

Lord Renwick

905. My Lord Chairman, I will go ahead with my question, but I think that what Mr Mehta has said has made me reconsider my question. However, I will put it because I do have some sympathy with the Commission as this is a very complicated form of scientific activity. I was wondering whether Mr Mehta could answer two questions. First, what level of expertise is there in the Commission to understand what the whole basis of biotechnology is and recombinant DNAs? Over the years, as he said, at the time of the preparation of these directives what range of consultations and of evidence was taken and what level of risks was being suggested to them for the need for such regulations? Can you give us a range from nil risk to great risk?

(*Mr Mehta*) My Lord Chairman, as regards the first question about expertise in the Commission, of course it has the necessary expertise, not only in our colleagues who are particularly responsible for these two directives but those who are working in related areas like, for instance, research and development because we have Community programmes on research and development which particularly link to risk assessment or link to various identified areas of genetic modification. Elsewhere as far as other products are concerned, medicinal, pharmaceutical and foodstuff we have had expertise for many years and they have been looking at this type of risk in the past anyway for other products. You must not forget that we also work in partnership with the Member State competent authorities, that is, with the expertise in the various competent authorities, namely environmental and health and safety executives: they meet and the issues are discussed with them and their experience and expertise is there. Then we have external experts whether they are from industry or from the scientific community. If you find that you are lacking any particular expertise then you go out and get it. As far as the question is concerned about what kind of risk we are looking at, if you look at the OECD work they identify what are the safety considerations to take into account. If you are saying you look for situations that are zero risk we know that situations with zero risk are impossible and you have to look at situations where the risks can be defined. What you try to do is to apply the regulatory approach to those situations where the risk is not negligible and you put into place various safety consdierations that have come over many years so that you are applying the approach that is commensurate with the risk shown. If you have a situation where the risk is significant it is clear that that would not be permitted. After all, to come back to your point about the scientific basis, my Lord Chairman, the directives do permit deliberate release and they do permit contained use whereas when the discussions started there was quite a lot of pressure that we should not permit at all this kind of technology. Until you are sure what are the risks and the long term effects the directive foresees that you have to take a precautionary approach in that respect.

906. So it is a continuing process, that is obvious, and therefore you are open to suggestions for an alteration and a modification. I do not think that in anything you just said commercial implications came in for the companies that are involved in this sort of activity. Do you take that into account as well?

(*Mr Mehta*) I am sorry, my Lord Chairman, I did not understand the question.

907. I will repeat it. Regulations obviously affect the commercial success or otherwise of the companies who are involved in this activity and we are looking at global competitiveness, which is the subject of our enquiry here as far as regulations affect competitiveness in various member countries and in member countries against Japan and the United States in particular.

(*Mr Mehta*) My Lord Chairman, I think if you are talking about deliberate release and whether we have a criterion of commercial productivity for companies, no, it is not there, that is not the purpose. The directive provides a framework. We have ourselves put a lot of stress on competitiveness. There was a communication of the Commission to Council and Parliament on competitiveness where we say that there are many other aspects that affect competitiveness. The regulatory framework is perhaps one, but it is far more important to innovate. This is a very important area. Why is it if you look at the patents that 60 per cent of them are in the United States? In the Community we are still ahead of Japan but we are far behind the USA. That is not because the regulatory framework alone is responsible. You have past innovations, research and development expenditure, you have the critical role that science

[Lord Renwick *contd.*]

plays and the capacity to encourage efficiency in research, you have the company size, you have the company capacity, the target and so on. You have to take into account all those factors, my Lord Chairman.

Chairman

908. You have just raised the relative strength of activity in the United States and Europe and elsewhere. Quite a number of witnesses have suggested to us that the regulations in the United States are much less restrictive than those in the EC. Do you agree with these witnesses?

(*Mr Mehta*) The Commission has also received submissions of this kind from industry. In response to that we have set up a group to look at it, the Biotechnology Co-ordination Committee, BCC, charged the various Commission services to look at these submissions. We have produced a report on the EC/US comparison, which I believe we have submitted to you, my Lord Chairman. That report has certain conclusions which are to be found on page 4. It comes clearly from this examination that, yes, there are certain differences. There are differences as regards scope, there are differences in flexibility and there are differences in procedure. We have 12 competent authorities—and I am now speaking about deliberate release for rDNA because, let us face it, that is where technology is still at the level of a lot of research and development work. In pharmaceutical sectors we have the commercial application. Again there if you look at the approvals of the Community you will find that you have a lot of approvals. Limiting ourselves to that therefore I think my answer to your question is that we think that regulatory frameworks are different, but whether you can attribute the entire difference in the development of biotechnology to that I think is an open question. What we put out was a consultation document, my Lord Chairman. We are looking forward to having views from industry and from others, and perhaps the report of this Committee, and we will take those into account in order to see whether we could conclude on that issue.

909. But some European industrialists, we are told, prefer to expand their activities in the United States rather than in Europe. They claim that this is becuase they find the regime there less restrictive. Does this cause you a certain amount of alarm?

(*Mr Mehta*) It is always of concern when there is an outflow not only of investment but of skilled manpower from the Community. I think that one has to take into account that in this sector as in other sectors the United States market perhaps offers much better potential for development than is the case here, and it is not because of the regulatory framework but because the markets have not yet developed in the Community. The pharmaceutical market in the United States, for instance, is bigger and more varied than here. In biotechnology the greatest or the most important commercialisation has been in that sector so it is clear that companies will go where the return is better. That fact alone does not mean that it is because of the regulatory system. You can look at the pharmaceutical industry in general, leaving aside the biotechnology part, and there again our companies have a very important share of the US market, and also in Japan, of course.

Lord Wade of Chorlton

910. I should like to put to Mr Mehta, my Lord Chairman, that in fact he seriously underestimates the impact of regulations. You seem to suggest, Mr Mehta, that regulations is one aspect, innovation is another aspect, the availability of finance is another aspect, but would you not agree that in fact at the start up of new businesses, the attitude of an entrepreneur depends enormously on how he sees the regulatory aspect of an industry and the availability of capital through venture capital and other investments is enormously dependent upon the regulatory aspect of the industry in which he might decide to invest? In other words, people have a choice in where they are going to put their money and where they are going to put their energies and they are naturally not going to work to one that they see unnecessarily regulated by outside forces that are not in full understanding of the industry and the opportunities. What also concerns me, my Lord Chairman, and I should appreciate having Mr Mehta's comments on this, is what appears to be the inordinate length of time from having to consider a regulation to actually implementing it. Now I accept that your directives have flexibility, but when you start talking as though you are talking to scientists in 1974 and it is ten years later before you are actually making any decisions on it, in a vastly changing industry where it is quite clear rightly or wrongly that the decisions that were made ten years ago are now seen to be obsolete do you feel satisfied that you are being able to change your attitude in order to allow the industry to expand as new knowledge be comes available?

(*Mr Mehta*) My Lord Chairman, the noble Lord has made several points and I will try to answer each of them. You say that the regulatory framework is important of course for the start up of business, but let us look at the facts. If you look in the Community we have something like 2,500 companies in biotechnology, and this is from a recent analysis of companies in biotechnology. The figures are quite interesting, my Lord Chairman. There are 2,500 companies in the Community, in EFTA countries there are 448, in the United States there are 1,073 and in Japan there are 347. The number of companies is not the only thing. There have been a lot of start ups in the Community and it is quite remarkable in different countries, for example, the United Kingdom has 700 companies compared with perhaps only 40 in Greece. As regards the regulatory framework itself you cannot say that this is the main reason you have more companies. It is then the question of size of company, how diverse they are, what markets they are looking at. If the markets are much wider and more dynamic then of course the companies will grow faster, their investment will be faster and so on. I think therefore that it is not simply a question of regulatory framework when you look at the start up of companies. As far as the availability of capital is concerned once again if it was not biotechnology I think everybody would agree that in other areas too venture capital and its availability is

[Lord Wade of Chorlton *contd.*]

perhaps greater in the United States than it is here. The links between the universities and private companies in the way they can do in the United States are much different. As far as access to the capital markets is concerned again there are more general questions not specific to biotechnology. My Lord Chairman, I should not like you to think that I completely disagree, that regulatory framework has no role at all. I think that it has a role but one should not at the same time exclusively focus on that. That was all that I tried to do. As far as implementation is concerned the directives were adopted by Council in 1990, October. It said that they should come into force by the end of 1991. We are today in 1993 and nine Member States have already implemented it because as a directive it has to go through national parliamentary procedure. It is the legal instrument that you use and Member States will adapt it to their own situation and use the competent authorities that are the most appropriate, and this takes time. I think we have experience with much Community legislation and where there is a need I think that there is a rapid change and here we have said that the Commission has looked at areas where one can make simplifying changes in the procedures. We have also said that we are ready to do so, my Lord Chairman.

Chairman

911. I should like to go on from your comment just now about making changes. Mr Bangemann said a week or two ago said that he welcomed proposals from the Member States. I wonder whether you could perhaps answer some fairly small questions for me. I think we will have to make this the last question, Mr Mehta, because time is getting on unless some of my colleagues wish to pursue this a little further. What I want to know is this. Apparently changes can be made by technical amendments or by simplified procedures. I am wondering what these are, Mr Mehta, and to what extent they require changes to the directives themselves rather than changes in methods of procedure.

(*Mr Mehta*) My Lord Chairman, as far as the scope of the directives are concerned this cannot be changed by this kind of technical change. The scope is laid down in the Council directive. If you want to change it you have to amend the directive. However, there are annexes to the directive which it is possible for the Commission using a regulatory committee to change. The importance of these changes is that when the directives are written and the annexes are there they are general. You can make an annexe which is specific to plants, the kind of information that industry would have to submit in order that authorities might do the risk assessment. That is the kind of change that we are talking about that can be done and that is under way in discussion. The simplified procedure is another possibility in the directive. What this does, my Lord Chairman, is to permit authorities which have sufficient experience to suggest ways to simplify the procedure for authorising deliberate release. This applies only to the research and development part, not to part C which is the placing on the market for the products of biotechnology. I think Mr Bangemann was referring to in his speech to Bio-Europe to Member States because the directive says explicitly that it is the Member State's competent authorities that would have to submit requests for simplification. We have received requests from France, from Belgium and from the United Kingdom, and they go in different directions, the communication between one authority and another authority in another Member State to notify, to simplify the notification, the information that you pass along, the distinction in information that is given between authority and operator, all these procedures can be simplified. However, they do not change the fact that those GMDs that under the scope remain subject to the directive remain subject to the directive.

Chairman] Thank you, Mr Mehta. I have no further questions.

Lord Soulsby of Swaffham Prior

912. My Lord Chairman, if I may raise just one quick point, since the conference of 20 years ago I think you will agree, and everybody does agree, that the United States has moved forward very quickly in the light of experience modified the approach to regulation. Since the evidence that people have to consider for modifications of regulations is international, not national, evidence is it solely that because of the somewhat complicated nature of the Community, namely, 12 competent authorities to consult making progress in the Community is slower, for example, than in the United States? If it is not that, Mr Mehta, what is the brake that is allowing the Community to go slower or, rather, forcing it to go slower than, say, the United States of America?

(*Mr Mehta*) My Lord Chairman, I believe that the situation is not just that there are 12 Member States. These directives come into force in 1991, and they were adopted in 1990. You have therefore a period which is much shorter for acquiring experience and also implementation for industry. In the United States they have a framework that was in place in 1986 or before that. They did something horizontal that was Tosca filling the gap and they had federal agencies and national institutes. You must take that into account. Where there has been a much longer experience, of course, it is also possible that the initial bugs have been sorted out. Finally, my Lord Chairman, what we also have to recognise—and this is the institutional point that you make—is that in the USA the administrator or the commissioner who is responsible for the Environmental Agency or the Food and Drug Administration or USDA can bring in interpretative rules after wide consultation which can change the way a regulation or an already existing one is applied. In the Community we do not have this flexibility. This does not mean, my Lord Chairman, that we cannot adapt nevertheless because I think that once you see five or six years of experience you will also see that what is under way will make the regulatory framework appear far more appropriate for industry. I think that industry must also themselves admit that when you have only a few years to work on a framework it means that you have initial adaptation problems.

Chairman] Mr Mehta, thank you very much.

Written Memorandum is printed separately

Examination of witness

DR SUSAN MAYER, Director of Science, Greenpeace, called in and examined.

Chairman

913. Dr Mayer, thank you for coming. First of all, I wonder whether you can tell us something about Greenpeace for the record—we have heard of it—and something about yourself and your scientific background?

(*Dr Mayer*) Thank you, my Lord Chairman. First of all I should like to thank you for giving Greenpeace the opportunity to give evidence to the Committee today. My name is Dr Susan Mayer and I am the director of Science at Greenpeace UK. My scientific qualifications are that I have two first degrees, one in pharmacology and one in veterinary science and my doctorate is in cell biology. I have been involved in Greenpeace UK in looking at the environmental implications of the technology of recombinant DNA, or genetic engineering and helping develop our policy in this area. As I am sure you know, my Lord Chairman, Greenpeace is an environmental organisation whose only interest is in the protection of the environment. We have in the United Kingdom 400,000 supporters and there are 4 million world wide. We have national offices in about 23 countries and our international headquarters are in Amsterdam. I should like, if I may, to define the limits of the evidence that we should like to give today and say first of all that they relate only to genetic engineering and not to biotechnology as a whole. That is because we do believe that genetic engineering is fundamentally different because it enables the genetic construction of nature to be altered in a way that can involve transgression of species' boundaries that could not occur in nature; and it fundamentally alters our relationship with nature. Therefore, it produces new and novel organisms that could not have evolved naturally. I want to say also, my Lord Chairman, that inside the area of genetic engineering our evidence is concerned with the release of genetically engineered organisms or GMOs to the environment. It does not, for example, consider the contained use of genetically modified organisms and the safety and desirability of drugs perhaps made in this way. Such medical applications are outside the expertise of Greenpeace to consider. Our feeling is that regulations concerning the rlease of genetically modified organisms have been designed to protect the environment and they have evolved in an atmosphere of there needing to be a precautionary approach to environmental protection, and this precautionary approach has been applied in the case of the release of genetically modified organisms because of the risk of there being potentially irreversible effects, which may multiply and there are considerable uncertainties, complexities and ignorance surrounding the issue. Because the constraints of evolution are lost there is a whole array of possibly damaging consequences. It is important to remember, I think, that the precautionary approach has been increasingly used in national, regional and international legislation and agreements. For instance, it was included in Agenda 21, which agreed at Rio last year. I think that the feeling there and elsewhere was that such an approach would be the only way that we should be able to attempt to achieve a sustainable future for our societies. Historically, the approach to the regulation of genetic engineering has taken the precautionary approach. It has recognised that in the case of genetically modified organisms the process by which they are produced has a direct hearing on their environmental impact although, of course, there may be other considerations to be taken into account. Therefore, my Lord Chairman, regulating their release on a process basis is vital if environmental protection is to be taken seriously. It would be illogical to do otherwise. It certainly seems sensible to keep that assessment under one expert committee which has seen the movement through trials and analysed the information and have the expertise in that area rather than perhaps splitting it up as might be the case if you moved to a product based regulation. Finally, my Lord Chairman, I should like to say as far as the claims for the environmental safety of the technology that are made, it is often said that our experience has been that the technology is completely safe. This is not really soundly based in science. There has been little or no assessment of the risk that environmentalists are concerned about taking place. Field trials have largely considered agronomic traits such as growth. The field plots are destroyed afterwards and the long term effects have not been addressed. Whatever the scale of the risks one of the fundamental questions relating to the technology which Greenpeace feels is particularly important is whether it is necessary, whether there is any justification for taking the risks that it involves.

914. Thank you. I gather that when you use the word environment you are really talking about nature. I am a civil engineer and I should use environment to mean something rather more than nature, a good deal of it "unnature", but let us leave that to one side. I think that that is what your main aim is?

A. Yes, it is.

915. And you suggest that some of the claims that have been made for genetic modification, which I prefer rather than engineering, have been exaggerated. Is it not the case that some of the fears of Greenpeace on other occasions have been exaggerated? I have in mind the tanker disaster in the Shetlands last year.

A. Earlier this year. I think perhaps that time will bear some of the answers to that. I think that it is far too early to say exactly what the impact of that oil spill has been. A spill of that scale certainly cannot have had no effect at all on the area so I think we will wait and see just what the case is in the longer term. It is too early to say yet, I am sure you would agree, my Lord Chairman.

916. I do agree, but Greenpeace in fact did not wait; they denounced the catastrophe before it

[Chairman *contd.*]

happened—but never mind. You seem to me to believe that the release of genetically modified organisms should not be sanctioned at all, is that right, if I read your evidence correctly?

A. Yes, that is right. Greenpeace feels that the risks of the technology, the risks of release to the environment, are such and threaten components of nature, which we value so highly so that we do not want to run that danger however small the risk may be.

Lord Gregson

917. Can you explain your philosophy with regard to the difference between genetically engineered products and natural evolution or human gene breeding?

A. I think that you can draw quite a clear line between what crosses may take place in nature between animals and plants, microorganisms of the same species.

918. Even if they are set up deliberately by human beings to make them happen mechanically?

A. Yes, but there is quite a difference in scale. There is no way in nature, for instance, that you could transfer a gene from a bacteria to a human or from a human to a fish.

919. That is one of the techniques; it is not fundamental to the manipulation? It is purely one of the techniques that are used. What is the difference? Take a plant from Mexico like breeding disease resistance into potatoes, take a plant from Mexico and bring it 8,000 miles across the earth and you spend ages dusting them and transpollinating them—what is the difference? Is there a real philosophical difference in that? It is interfering with nature in a major way?

A. To say that there are special and different dangers with genetic engineering is not to say that there are not dangers with the import, say, of exotic organisms or other agricultural processes that may occur. That is undoubtedly the case. But there is a difference, I believe, when you cross species' boundaries and when you are doing it on a time scale that is so short that you have lost some of the constraints, some of the timelessness, if you like, that take place in a more natural so-called traditional breeding technique. You simply lose that with genetic engineering so I think that it gives us a very different series of dangers, and we must take those very seriously.

Lord Walton of Detchant

920. My Lord Chairman, perhaps I may just follow this up. You are of course no doubt fully aware that two high level committees in the United States and in Japan, both with powerful scientific and lay representation, came to the conclusion that the alleged risks of genetic engineering to human health and to the environment had been grossly exaggerated. I should like to follow this up, my Lord Chairman, by just making a couple of points. When you say that claims for genetic engineering benefits are purely hypothetical, I wholly appreciate that you say that you are not dealing with, for example, medical use, but insulin has been produced by genetic modification as have other pharmaceuticals. Monoclonal antibodies are widely used in diagnosis and now gene therapy for single gene disease in humans using bacterial or viral vectors has become a reality. Do you really feel that these advances are purely hypothetical?

A. When we are talking about the release of genetically modified organisms there has been none that have come to the market and been proven and been useful. As I said, I am putting my evidence down in terms that the evidence of Greenpeace is looking at the release of genetically modified organisms to the environment, and that is what we are considering. But I should like perhaps go on to try to answer your question a little bit better. Implicit in the claims that genetic engineering is essential for development in the future, so that we can all benefit from it, is that there is no other way and if we do not use that path we are somehow blocking society. I should like you to consider that there are, in fact, other paths that will take us down a more environmentally sustainable future that we could look at, so simply not using one path does not mean that you are going against any type of development or any type of industrial application in other areas. If you would bear with me for a moment, because I think that it is an important and worryingly narrow way of thinking that may in fact close down opportunities for industry if we take that line too far, my Lord Chairman, I should like to give you an example from another area where Greenpeace has been involved where I think that we have helped open up that narrow way of thinking. It will seem distant from what we are talking about now, but I will bring it back to genetic engineering. I am sure that you are probably all aware that ozone depletion has brought out the need to find alternatives to CFCs in refrigeration and insulation foams. Mainline thinking on the alternatives that were being offered for that were HCFCs and HFCs, for instance. HCFCs deplete the ozone in the short term, HFCs are powerful greenhouse gases. Greenpeace felt that with the situation as regards climate they were not suitable alternatives. What Greenpeace did in Germany was to put together two research scientists and an ex German fridge company—and I should like to emphasise that this was only last year—who have developed a fridge using a propane/butane mixture as a refrigerant. That was, if you like, a neglected refrigerant; it had been on the back seat and had been largely ignored. That fridge has been developed to a stage where it is now available commercially. Large fridge companies now in Germany—Bosch and Siemens—have actually taken on those ozone safe fridges and are marketing them in Germany and in the United Kingdom at the present time. Greenpeace took the fridge to China recently and it seems as if the technology will progress into that area.

Lord Gregson

921. How certain are you that the refrigerant is harmless?

A. What I should like to say is that what we can do is to make choices. We can look at choices as to what we think will be environmentally safe. I should not like to claim that any technology is environmentaly

[Lord Gregson *contd.*]

benign at all, but when we are weighing up the risks of ozone depletion with some other effects I think that propane/butane mixture seems to be a better bet in the short term, and—

922. But you do not know.

A. There has been considerable long term experience with propane butane.

923. You do not know, do you?

A. No, and that will apply to a lot of other areas where—

924. As it applies to the subject that we are discussing today?

A. It will apply exactly to the subject that we are discussing today: we simply do not know what the impact of genetic engineering will be, and that is really one of the cruxes of the issue. However, my Lord Chairman, I should like to go on from that to say that Greenpeace in the United Kingdom developed a similar fridge with scientists of what was South Bank Poly last year and tell you what has happened. United Kingdom industry has not taken up that challenge. The new German fridge is going to be available in the United Kingdom with quite an environmental selling advantage, and it has now, for instance, won energy efficiency awards. That took about a year and an injection of alternative thinking, if you like. As you say, it may have problems in the longer run but we think that it is another way of thinking about things. It gives you a different alternative, it takes you down a different path, and those things people should think about and agree. But to bring it back to the issues that we are thinking about, on occasions I think that we should think about what might be achievable if the resources being devoted to genetic engineering were given, for instance, to develop organic agricultural systems. We could have much better mechanical weeders, for instance, or we could have new crop rotations that would help combat disease. Not taking the genetic engineering path therefore is not a negative step necessarily. It may mean opening us up and industry up to much wider opportunities. In these days where people are much more sensitive and have a greater desire and understanding to protect the environment those are the challenges that I should have thought industry ought to take up and in which they ought to see a very rosy future.

Lord Walton of Detchant

925. With respect, my Lord Chairman, may I just complete the point that I wanted to make. I wholly appreciate that you are not dealing with medical issues, but if it were shown, as seems likely, that the only means of introducing a gene into a human subject suffering from a fatal progressive disease were to use a proven harmless viral or bacterial vector which thereby would be released because it would be introduced into the individual, if there were no other mean of treating that condition, which is of course genetic manipulation, do you mean that Greenpeace would oppose it?

A. My Lord Chairman, what I am saying is that I hope would think very carefully about the wider implications and consider if it was to involve a viral vector which was living and to be released into the environment whether there would be serious considerations for the environment and for other humans presumably that should be taken into account.

926. You can be assured that those issues are being taken fully into account. The question is, would Greenpeace oppose it?

A. We do not as a rule because we have not got an expertise in the area of health. It is not an area that we cover. I think that it would be inappropriate for me to talk about health issues when it is outside our expertise.

Chairman] It is, I think, more a philosophical question than a medical one.

Lord Soulsby of Swaffham Prior

927. My Lord Chairman, I should like to follow up the line that Lord Walton has developed. In your submission you say that your particular interest is the environmental importance of the industry in relation to the release of genetically modified organisms and that you do not wish to deal with the wider issues such as medical, but indeed to develop the areas of medical use does involve industry: it is industry indeed that has got to be convinced to make the vaccines and new developments and without industry taking an important role in this no medical developments would get to the population at large. So much of the new developments for the prevention of disease in man and in animals in nature—because nature is really an integration of many things, often man made integration, and the welfare of man and his animals I am sure you would appreciate and that health of these is important. Already we have release of genetically modified organisms. An example is the rabies vaccine which has been used in Europe which is very highly effective. It is a genetically modified organism and there are a number of other vaccines for veterinary use at least that are based on the release of viruses that have been crippled in knowledgeable ways so that they cannot then invade other viruses and change them. All of these are part and parcel it seems to me at lesat of preserving the sort of nature that you are talking about. If nature is going to be exposed to pandemics of disease periodically which they are and we have ways of dealing with them by the release of carefully controlled organisms genetically modified that would seem to be a very logical, reasonable and civilised way of dealing with it. Would you disagree with that?

A. Dealing with disease and wild populations be it through vaccinations or other mechanisms is actually a very difficult thing to do and it is not often very simple. Vaccination is not necessarily either a better answer or the only ansewr to that problem. I think that it is a little bit unfair to suggest that we in our approach to genetic engineering are suggesting that we are posing a future that involves the spread of pandemic infections through the world, because that simply is not the case at all.

928. No, I am sorry, I was talking about the prevention of disease rather than creating it.

A. I am going to go back to my earlier answer when I was trying to convince you that there are very often—in fact, I think that it would be almost

[Lord Soulsby of Swaffham Prior *contd.*]

impossible to find a case where there was not an alternative and there were other ways of doing things. That is one crucial change in our thinking that I think has got to come about if we are to have a sustainable future. It is not always the best approach to take what is the most obvious or seemingly the most simple. That has not necessarily been the most successful in the past. Therefore, I do not think that it is fair to say that becuase you are saying this may not be the most appropriate path to take you are therefore saying that there is going to be more disease. That just is not necessarily the case.

929. Perhaps I may have just one final comment here, my Lord Chairman. Let us be quite specific and let us take rabies, for example, in foxes. The rabies vaccine is 98 per cent effective and probably 100 per cent. The only alternate to prevention of rabies in foxes is to kill foxes. It is a balance of, would you wish that to happen or would you wish the recombinant vaccine to be used?

A. As I understand it, the recombinant vaccine is still under trial. There is a live vaccine that is under trial at the moment, that is right, is it not, not the recombinant vaccine?

930. Well, it is both.

A. Still under trial.

931. No, used on 100,000 foxed or more foxes in France at present.

A. But the new live vaccine is not licensed for sale, for instance, for use in the United Kingdom or other parts of Europe, as I understand it, at the moment, is it?

932. It has been used by European governments.

A. But it is still under a process of being assessed, as I understand it.

933. No.

A. It is commercially available?

934. Well, yes, but it does not need to be commercially available if it used for control on a national scale by the appropriate governments.

A. I do not want to enter into the specifics on that one because I do not know the specifics of that case sufficiently to discuss it with you. But I should just say that we have to think very carefully about this type of issue and assess fully whether these are being as effective as they are claimed to be when you are using vaccines to control disease in wild populations.

Chairman

935. There are two ways of looking at that. You are quite right, of course, when you say that these things should be considered carefulluy to see whether they are as effective as they are claimed to be. However, the other side of that coin is that they should be assessed very carefully to see whether they are as dangerous as some people think that they are. It is the same sort of thinking that you have been putting forward, is that not right?

A. And also that you should look at what alternatives there might be and developed equally well and not always just take one path. You must keep open to there being alternative solutions.

936. You might have to make up your mind just once in a while.

A. You might indeed, yes, but you should not necessarily from the outset have a predetermined outcome of the discussion.

Lord Wade of Chorlton

937. My Lord Chairman, I am a layman and I have been listening to the evidence. We have obviously had a lot of evidence from very capable scientific peole who have been able to explain clearly in scientific terms why they are satisfied that certain of these technologies are safe. You are telling us that they are not safe, or that you believe them not to be safe, yet you do not seem to be able to give us any scientific evidence as to why they should not be safe. It appears to me from what you are saying that you believe that they are and you do not want to take any risks or it might be this way or it might be that way, yet we have had very, very sound evidence from people highly experienced and knowledgeable in these matters who are very clearly on scientific basis convinced that evidence has shown them to be safe. Can you give us any sound scientific reasons for you to feel insecure or frightened of what this technology might do to you or me?

A. Yes, I am very happy to do that. First of all though I should like to say that I also know that evidence has been presented to the Committee which has underlined that it is a new process, it creates novel organisms that do pose particular risks of their own to the environment, and they—

938. Give me one.

A. Professor Williamson, Dr Kinderlere, Professor Polge, did say that it was a new technology and it did create new organisms and imposed certain risks, and they—

939. But they also made very clear that in their view the risks were very, very, very slight. Are you saying that you are not satisfied to go into any future life at all unless you have eliminated all your risks or do you believe that in all life we have to accept certain risks, no matter what we do? Or do you have a system that eliminates risk?

A. I will go on to answer you in two ways. The first is to say that I hope that you have asked scientific experts whether they feel even under our current regulatory system there will not be a situation that will arise where there will be serious problems and—

940. What we have asked the others is history. It is you now and I want to understand what you believe.

A. We have looked at the evidence and we believe that there is not a way that you can predict how these new organisms will behave in the environment. We also do not believe that those risks have been looked at properly, that issues of safety have been looked at properly, and we think—

Lord Wade of Chorlton] I am sorry, you keep missing the point that I want to make.

Chairman] I think you really should let the witness complete what she is saying.

Lord Wade of Chorlton

941. You are going away from the point I am asking you about.

A. For instance, let us think about weediness. One of the issues that people raise is that of weediness. Some scientists, though others would disagree with it, would say that there has been no evidence of weediness through all the trials that have been done in the past. I should like if I may to quote to you from Nature of 17 June, an observation on a paper in there which says: "So although more than 300 field trials have been carried out and no evidence of weediness has yet emerged that should not be interpreted as an especially comforting observation. We have been so thorough in containing or destroying all materials in field trials that we could hardly expect to see any hint of problems from these studies. The real question is what will happen when transgenic seeds are widely broadcast year after year in many habitats as would be the case with genetically engineered crops planted commercially". I think that shows you the limitations of scientific understanding and the way that scientific experiments have been carried out in the past. They simply do not have the answers to those questions. I think that I also tried to make it quite clear that Greenpeace values the integrity of nature, if you like. We find it an unacceptable danger that there could be a genetic pollution of natural organisms. There is no way, we believe—and we have consulted scientists—that they are going to be able to do full safety assessments that would assure us that that would never happen. Therefore, we do feel that you can say on a purely scientific basis that because you cannot quantify that risk—sometimes it will be very small and sometimes it might not be very small—if you are not prepared to take the danger that is the position that we take, and I think that that is morally and scientifically justifiable.

Lord Gregson

942. No endeavour of mankind is without risk. You cannot live on this earth without risk. You have to take risks to live.

A. We are not denying that—

943. With the world population that we have now got and that we are getting we have to take very definite steps to make sure that we can feed them and look after them. It cannot be done by nature alone.

A. It certainly cannot be done by genetic engineering.

Lord Gregson] How do you know?

Chairman

944. Hang on, I think that we are getting into a series of arguments here rather than examination of a witness, and I think we should contain ourselves. May I ask a question—and I mean that the Committee should contain itself, not the chairman! In the course of your evidence, Dr Mayer, you have referred once or twice to the 13th report of the Royal Commission on Environmental Pollution, talking about risks and so on. In the course of that report the commission said that "we see no environmental justification for preventing releases that are considered safe from proceeding". My question must in the nature of things be hypothetical. I am assuming that a sufficient time has eapsed for something to be considered safe having been properly examined by proper scientists of all persuasions. If it came about that certain relases in your field were considered safe would you still say that these things should not be released?

A. At the moment, my Lord Chairman, I think that that would be our position. We have seen no convincing evidence that would suggest that any of the claims of safety to date are soundly based so that with the type of experiments that are done and the types of changes being made to different species I cannot foresee a change in that approach.

945. You do not think that a situation could arrive in which certain releases were considered safe to such an extent that you would be satisfied that they were safe?

A. I think that the uncertainties and ignorance that surround our knowledge in this area are so huge that I cannot conceive of that situation happening.

946. Not even in a while?

A. I should just like to emphasise again that our ignorance of the behaviour of species, of the natural environment, is so huge that I really do not think that we will get to that stage. I think that it is really important as well to ask what the justification for running such risks is. We see no justification for taking those risks.

947. I see—oh, well. Are there any further questions. I have only one final tiny question. In paragraph 4 of your evidence you list four risks that are possible. Unfortunately, you have included the creation of new pests twice.

A. Yes, I am sorry about that.

948. Presumably the fourth is something else, and I was wondering what it was. Do you remember what it was?

A. I am afraid that I cannot remember what the fourth one was.

Chairman] Don't worry.

Lord Gregson] Perhaps you would like to drop us a line if you can recall it.

Chairman

949. And in dropping a line do not restrict yourself to that minor question that I have just raised. If there is anything that you wish to add to the evidence that you have given today having thought about it we should like to hear that too. Thank you very much, Dr Mayer. We should not have considered completing our report without asking people such as yourselves.

A. Thank you.

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WRITTEN EVIDENCE

Written Evidence Received after 30 April 1993

Evidence from the Advisory Board for the Research Councils (ABRC)

1. *What is your interest in biotechnology?*

The ABRC has an overarching interest in the subject and has a Biotechnology Sub-committee. This Sub-committee produced a report in the summer of 1992 and now keeps a watching brief, ready to advise the Board should issues requiring action arise. In addition, all five of the research Councils fund research in biotechnology or related subjects. The specific nature of their activity is explained in their independent submissions and is evidenced by their individual membership of the Biotechnology Joint Advisory Board. The Chair of BJAB meets the Board annually to discuss BJAB's projects and plans.

2. *How and why is biotechnology important to UK industry?*

Biological systems have achieved very efficient solutions to a host of problems by operating a very rigorous process of evolution through natural selection that is on an immense timescale compared with human technological innovation. Exploitation of knowledge of such systems for the purposes of innovation in industry, healthcare, environmental monitoring and protection as well as many other areas has already yielded immense returns. An example from the pharmaceutical industry might serve to illustrate the point. Many pharmaceutical products have two rotational isomers only one of which is metabolised by the human body. Pharmaceutical chemists often find it difficult, using standard synthetic mythods, to isolate the pure isomer uncontaminated by the other isomer or isomers which differ only in chirality from the desired product, whereas biological methods have solved the difficulty because the enzymes or organisms used may be engineered to produce only the required isomer. These biotechnological methods are now an essential part of many sectors of industry and healthcare in the UK. Since our understanding of biological systems is still very limited we can confidently anticipate that the scope of biotechnology will continue to broaden with advances in the basic biological sciences. The relationship between academic biotechnology and industry is a reciprocal relationship. A healthy science base assists industry, among other things by producing scientists appropriately trained for employment, and in return, industry is vital in helping to sustain the science base.

3. *What future prospects and opportunities does the technology offer?*

As the ABRC Biotechnology Sub-committee report (1992) states in the executive summary: "Biotechnology is not a scientific discipline, but rather an expanding collection of technologies based on scientific advances". A wide range of technological developments have already taken place which have mostly emerged from advances in current knowledge. Examples of these include genetically engineered animals and plants, the production of medically and scientifically useful nucleic acids, proteins and other reagents and improvements in techniques used in *in vitro* fertilisation (IVF). For the future, in the shorter term, developments might well seek to answer particular questions. For example, the production of kits designed to identify individual genes or packets of reagents for use in the clinic, enabling diagnosis of specific diseases more or less instantly. Given the rapid progress in basic research, it is becoming increasingly difficult to make predictions for the longer term, although biotechnology will undoubtedly assume growing importance in an increasing number of areas.

4. *Which developments in biotechnology raise issues of safety and how should they be addressed?*

With the introduction of new techniques and organisms into the laboratory, either by industry or in academia, the safety implications must be considered carefully. Any developments involving new techniques or modified organisms carry potential risks and uncertainties that require careful evaluation. It is important to have regulatory structures that ensure prompt evaluation while being flexible enough to change when, as often happens, the risk is found to have been over-estimated.

5. *Should biotechnology be regulated by an industry specific regime?*

These biotechnologies may be of use for many different industries, for example Amersham International, a company known for production of radiolabelled chemicals, gains considerable and increasing revenue from the sale of molecular biology kits and reagents. In addition, in the healthcare sector new treatments may be taken straight from the laboratory to the patient without involving industry (an example is new treatments for infertility), so that an industry specific regime would not regulate them.

6. *From a technical point of view, is horizontal regulation better than vertical regulation?*

One mode of regulation may not be appropriate, see point 5.

7. *Should regulation evolve from a horizontal to a vertical aproach in each industrial or environmental application?*

8. *How do current regulations compare with those of other competitor countries?*

The comparison varies according to the specific techniques; for IVF, the UK is among the more liberal countries.

9. *What are the consequences, or likely consequences, of the regulatory regime on competitiveness of the UK industry, in particular as regards:*

research
product development
investment
location
sales and marketing?

Many biotechnology companies, and companies using biotechnology, are multinational and, for research purposes, will locate themselves where-ever the regime allows them to function most satisfactorily.

10. *Is there a danger that the present regulatory regime will prevent the exploitation by British industry of research conducted in the UK science base?*

Regulatory regimes must be flexible enough to move their policies in line with the most up-to-date knowledge and should not be bound by redundant rules.

11. *How best can issues of public acceptance be addressed?*

People need to be informed about the issues in an unbiased way and the machinery to do this needs to be put into place. The ESRC's relevant research on such subjects as risk perception should be used to ensure people are informed rather than persuaded and that the levels of jargon are reduced to a minimum. Schoolchildren should be addressed and encouraged to debate the issues, these are the future adults. Informing the public more widely is an issue which crosses the whole of science. Biotechnologists could learn from successes and problems found in other fields of science which have had a high public profile such as IVF and the use of animals in research.

12. *What other factors do you consider will play a crucial role in the competitiveness of the UK biotechology industry?*

The mutual benefits that accrue from a healthy biotechnology industry cannot be overemphasised. Industry requires both the highly trained manpower and know-how that the science base can provide. It is therefore no coincidence that the biotechnology industry is most healthy in those countries that have a strong science base. Reciprocally, because of the pervasive nature of molecular techniques in modern biology, the science base is crucially dependent for its competitiveness on the availability of high quality biochemical reagents and kits that the industry can provide. It is difficult in these days for a basic science laboratory to maintain a competitive edge while preparing most of the essential enzymes and other reagents that are required. If there is no home-based industry then these reagents will have to be obtained from abroad.

Evidence from the Association of the British Pharmaceutical Industry (ABPI)

1. *What is your interest in biotechnology?*

The Association of the British Pharmaceutical Industry (ABPI) is the trade association representing the majority of the pharmaceutical companies in the United Kingdom who are engaged in discovering, developing and manufacturing prescription medicines. A number of our member companies, including Glaxo, British-Biotechnology plc, Hoechst, Zeneca Pharmaceuticals and SmithKline Beecham have already given evidence to this present inquiry.

Many of the Association's members consider biotechnology to be a technology fundamental to their activities, and see the application of biotechnology as playing a key role in the development of new treatments for human disease. The Association's members include those who use biotechnology only at the Research and Development stage, or in contained facilities in the production of well established therapeutic products eg, insulin, human growth hormone, antibiotics etc.

New developments using the tools of biotechnology are in the pipeline and it is likely that products that contain genetically modified organisms eg, vaccines will be available in the near future. Some of the areas of the pharmaceutical industry's current interest in biotechnology include:

Drug Discovery in the 1990's requires more than ever a molecular insight into the functions of the cells and tissues. The skills of those trained in biomedical research, in molecular biology, cell biology and protein biochemistry (the new biotechnology) now complement the more well established research disciplines such as chemistry and pharmacology in the pursuit of effective novel therapies for the unmet clinical needs of the 20th Century and beyond.

Therapeutic Protein Research employs biotechnology to produce usable quantities of naturally-secreted proteins (hormones, human receptors, cytokines, enzymes, antibodies etc) for therapeutic evaluation. Furthermore the study of such substances gives leads to design of modified analogues which can offer improved therapeutic characteristics.

Alternatives to the use of whole animals in the discovery of drugs through the use of cell-based assays *in vitro*. This reinforces not only the highly important shift towards *in vitro* screening but also permits greater throughput in screening for novel active agents without necessarily sacrificing a very large degree of specificity.

Transgenic animals can be used for the production of therapeutic proteins, of customised cells or to facilitate testing of potential new medicines.

Gene Therapy is a rapidly expanding area of science which is at the forefront of technology. Both academia and industry are currently evaluating its potential for therapeutic intervention in a range of human diseases and genetic diseases. Now that the UK is moving towards the establishment of an appropriate regulatory process rapid advances are anticipated in the UK.

Manufacture of development and production quantities of biologically active molecules which are not readily available by other means, through cell culture and fermentation. These biopharmaceuticals include therapeutic proteins eg growth factors and monoclonal antibodies.

In addition improvements will be made to conventional microbial technology for the largescale production of antibiotics

2. *How and why is biotechnology important to UK industry?*

The Association can only comment on the growing importance of the use of biotechnological processes and techniques to the competitiveness of the pharmaceutical industry. The British pharmaceutical industry has consistently been one of the most successful sectors of industry in the UK over the last 40 years, and is considered to be one of the most innovative industries in the UK. Five of the world's 20 most prescribed medicines are British. Medicine exports from the UK are worth nearly £3 billion a year and in terms of manufacturing trade balance are the second largest foreign exchange earner for the British economy.

The pharmaceutical industry currently spends £1,400 million a year on the search for new and better medicines. The pharmaceutical industry is an internationally based industry, and in addition to British companies, many of the companies established in the UK are from the rest of Europe, the USA and Japan. In addition to the regulatory and financial environment, an important factor contributing to the willingness of transnational companies to go on increasing their investment in biomedical research in the UK has been the high quality of the research carried out in its universities, research institutes and medical schools, and the availability of well trained, innovative scientists emerging from British universities.

The UK has particular strengths in basic research in biochemistry and biomedicine going back to early work on the structure of DNA and the discovery of monoclonal antibodies. Through the continuing close collaboration of academia with the pharmaceutical industry, such expertise will continue to make a significant contribution to the country's competitiveness.

As well as becoming an essential skill in the carrying out of existing processes of drug discovery, biotechnology represents a route to the production of novel biological products which can be used in the treatment of disease. Through biotechnology the production of proteins can be carried out in a variety of different host cell types. Compared with those isolated from natural sources, recombinant proteins can be human in origin and can be produced in large quantities and a relatively low cost. Most importantly they can be produced in a manner and from a source whose safety can be assured. This has been shown to be particularly important when the only natural source of the protein was previously a scarce or diseased tissue which may be contained with potentially lethal, infectious agents (eg Creutzfeldt-Jacob disease arising from human growth hormone). In addition, the techniques of biotechnology enable natural proteins to be engineered to futher improve their potency and selectivity, to reduce unwanted side effects or to make them longer acting, more stable on the pharmacists shelf or more readily or effectively formulated (eg as a depot formulation).

Exploitation of biotechnology to provide access to recombinant proteins is of increasing importance to the pharmaceutical industry. A number of proteins have been commercialised as therapeutics in their own right; more importantly, the availability of others is facilitating the discovery of small molecule drugs. In several instances a protein is the only route to therapy in a particular disease (eg insulin therapy for diabetes, growth hormone therapy for pitutary dwarfism, erythropoeitin therapy for anaemia). In other cases proteins can be used to extend existing therapies to make them more effective (eg the administration of G-CSF to reduce the dose-limiting neutropenia associated with cancer chemotherapy).

The production of these sorts of compounds on commercial scale is an extremely high risk enterprise in which the prevailing regulatory climate has major influence. Considering the unparalled contribution which UK academia has made to fundamental biomedical research, capital investment in biotech production plant remains remarkably low. Despite an excellent scientific environment and the relatively low cost of doing and applying science in the UK, much of the world wide investment in biotechnology manufacturing is going elsewhere. It is essential that the UK attracts and retains this manufacturing within the country.

In the last ten years a number of specialist companies including Celltech, British Biotechnology, Delta Biotechnology, Scotgen have been established within the UK to take advantage of the opportunities presented by biotechnology in the medical arena. Established pharmaceutical companies have also expanded with similar objectives. These activities have contributed jobs to the economy and exports to the balance of payments.

3. *What future prospects does the technology offer?*

Within the pharmaceutical industry the tools of biotechnology are seen as major sources of innovative approaches to the treatment of disease and improving human healthcare. Some of the wide-ranging possibilities include:

(i) *Improvements to drug discovery techniques*

Techniques are being developed for the identification of targets for therapeutic intervention. Through DNA technology companies are now able to screen for novel agents which interact with the particular human receptor or enzyme of interest. Using such cell-based assays, companies will be able to search rapidly through many compounds which could lead the way to important new therapies. In addition, recombinant human proteins can be produced in sufficient quantities to provide research reagents which can be used to explore structural features responsible for the selectivity of the molecules. Biotechnological techniques will also allow researchers to investigate the changes in gene expression which contribute to disease.

(ii) *Gene therapy*

Developments arising from the Human Genome mapping project and the associated gene sequencing initiatives are leading to an understanding of the genetic basis of disease. This work will lead to the possibility of therapeutic intervention by conventionally produced products, or by those produced by biotechnology processes. This work is also leading to novel gene therapy applications of inherited diseases. Such gene therapy is becoming will established in the USA, but has only recently started in the UK following the recommendations of the Clothier Committee.

(iii) *Improved access to therapeutic proteins*

Most medicines available today exert their effect by interaction with proteins in the body. The majority of these medicines have been discovered by random screening of natural compounds or collections of synthetic chemicals. In the future as biotechnology contributes to an increased understanding of medical science, the use of natural and engineered recombinant proteins as specific therapeutics against a variety of diseases will continue. The sensitivity of protein structure analysis will be further improved such that analysis of the final protein product, rather than the consistency of the production process will become the more reliable guarantor of product quality. Also, greater understanding of protein structure will have increased impact on the effective rational design of synthetic chemicals either as agents active against protein targets or as orally active mimetics of protein effectors. A pharmaceutical company without strength in these areas will be increasingly disadvantaged as global competition intensifies.

Other opportunities include:—

(iv) The development of novel and more effective vaccines

(v) The development of novel biopharmaceuticals, including monoclonal antibodies

(vi) The use of biotransformation for the resolution of chiral mixtures and the production of important enzymes.

(vii) The development of clinical diagnostics (Cancer, Aids).

(viii) Improvements to the yield of established fermentation processes through the use of genetically modified organisms.

(ix) The development of antisense drugs (ie, DNA or RNA sequences that bind to and mark specific gene activities) for the treatment of certain cancer/viral diseases.

4. *Which developments in biotechnology raise issues of safety and how should they be addressed?*

As an industry where the safety and quality of the product is of paramount importance, the pharmaceutical industry is one of the most regulated industry sectors. Within the existing regulatory framework all safety aspects of working with biotechnology have been, we believe, adequately addressed for many years.

At the *Research and Development* stage safety issues, particularly those relating to worker safety, have been handled effectively through legislation such as the Health and Safety at Work Act 1974 (the HSW Act), the Control of Substances Hazardous to Health Regulations (COSHH) and the Genetic Manipulation Regulations 1989. We now have the Genetically Modified Organisms (Contained Use) Regulations. The earlier Genetic Manipulation Advisory Group, (GMAG), and subsequently the Advisory Committee on

Genetic Modification (ACGM) have provided an expert forum at which scientific advice (and approval) can be given by a broad mix of scientific regulatory and lay representatives. The HSE's ACGM have also published a series of detailed guidance notes on individual subjects related to work with Genetically Modified Organisms.

Such experience would develop along the lines of work with unmodified organisms, which are controlled by the corresponding ACDP guidelines which are currently less restrictive than the new genetic manipulation "contained use regulations" despite the fact that genetic manipulation work is normally based on *disabled* micro- and non-microorganisms and *known* gene sequences of known properties. For example, ACDP notification is only required for certain category four pathogens in contrast to the new genetic manipulation notification required when category two organisms are involved.

We consider that the majority of the basic gene modifications carried out at the laboratory stage present little hazard. The technology is now well understood and has been well worked out over the last 20 to 30 years. However, the ability to transfer genetic material between different species and the possibility of such organisms having the ability to self replicate does raise specific safety concerns, and such modifications are carried out under appropriate levels of containment.

At the *Manufacturing* stage the HSE legislation, continues to apply with particular emphasis being paid to the protection of staff. HSE inspectors have extensive powers of inspection under the Health and Safety at Work Act and can enter premises, require the provision of information relevant to their proposals. The HSE has built up considerable expertise in the assessment of risk-categorisation over the many years the industry has been using such techniques. The GMOs used in the large scale production of therapeutic products have generally been selected so that they are unable to survive outside the containment facility, and when required are inactivated and destroyed prior to disposal.

The safety assessment of *Products* involve all aspects of the R&D and manufacturing stage. Comprehensive EC and UK rules exist for the approval of a new medicine before it is placed on the market. In the UK, this involves the grant of product licences under the Medicines Act 1968. The safety testing of all products intended for use in patients involves an assessment of its quality, safety and efficiency, and includes exhaustive toxicity testing, sterility testing and quality checks to ensure the purity of the product and that it is free from harmful containments. The quality and safety of the starting materials used in production are tested, and the manufacturing process is continuously monitored. Companies are routinely inspected to see if they are complying with the provisions of their product and manufacturing licences, and are complying with Good Manufacturing Practice, Good Laboratory Practice, and Good Clinical Practice.

Ethical issues relating to the use of gene therapy were, we consider, adequately addressed by the Clothier Committee. It is understood that an expert Advisory Committee is to be established to provide advice and a regulatory framework for future work in this area. The Association strongly recommends that such a committee should have access to experts with a thorough understanding of the scientific and technical aspects of gene therapy.

For some time to come, until the development of medicines that contain GMOs, eg, novel vaccines, the majority of the pharmaceutical industry's biotechnology activities will relate to the Contained Use Regulations, and not to the Deliberate Release Regulations. Both Regulations were implemented into UK law in February 1993 and it is possibly too early to say whether they will in fact improve the safety assessment of biotechnology work in the UK.

5. *Should biotechnology be regulated by an industry specific regime?*

This question can be interpreted in a number of ways.

If the question is inferring that there should be a regulatory regime for the biotechnology-industry then our answer would be emphatically no. As other industry experts have pointed out to the Select Committee, the Association strongly believes that there is no biotechnology-industry *per se*, but a number of specific industrial sectors (pharmaceuticals, agrochemicals etc) making use of the technology. Within the pharmaceutical industry the wide variety of techniques and processes which make up biotechnology are an essential part of its overall activities.

There should be, and there is, a pharmaceutical industry specific regime for the regulation of products, whether developed by biotechnology or by other methods. Medicinal products are already regulated for their safety, quality and efficacy. Each product raises unique safety and benefit/risk questions which we believe can only be addressed by Health Authorities as part of their evaluation process. The sectoral based regulations will continue to evolve to accommodate new technology if it changes the essential nature of the product.

Except in the circumstances where it does impinge on the specific/product legislation, and thus causes duplication, we consider that the regulation of the biotechnology process *per se* has been appropriately conducted under existing safety legislation. It is to be hoped that in time a similarly intelligent approach, based on scientifically-proven assessments will be established with respect to environmental legislation.

6. *From a technical point of view, is horizontal regulation (where a product is judged through the process by which it is derived) better than vertical regulation (where a product is judged by its characteristics).*

Medicinal products are regulated through a vertical process which assesses the quality, safety and efficacy of the product. All aspects of the production of the product are assessed including the quality of the starting material, the safety testing of the product, the premises in which it is produced, its efficacy and its risk/benefit relationship. Current UK regulations are in accordance with the specific European Directives. This vertical assessment is handled by an agency (MCA, CPMP) which can make a judgement in all aspects of the product.

Horizontal regulation applies to processes where there is no specific product, ie, in health and safety in the workplace legislation.

The key question is whether the trigger for the regulatory review should be the act of genetic modification or the product. There are three broad levels for the regulation of biotechnology; laboratory research, the development period (trials etc) and placing a product on the market. The first can be realistically regulated by the techniques being used in these situations. However, once one has actually used the technique to produce a potential product then there is a clear difference of opinion. The European Community produced Directive 90/220 which uses as a trigger for regulatory review the act of genetic modification. The USA have adapted existing safety legislation to deal with the development and marketing of products produced by genetic modification.

Imposing a horizontal regulatory approach upon a vertical regulatory system does not lead to an increase in safety for human health or the environment, but does lead to unnecessary duplication.

7. *Should regulation evolve from a horizontal to a vertical approach in each industrial or environmental application?*

EFPIA (The European Federation of Pharmaceutical Industry Association) of which the ABPI is a member, attempted from the start to have pharmaceuticals excluded from the provisions of the horizontal legislation embodied in the EC Contained Use and Deliberate Release Directives, but was not successful. The pharmaceutical industry requirements should—in the pharmaceutical field—be the object of controls applies with the vertical competence of health authorities (eg, Medicines Control Agency). Gives the distinct and specialised nature of medicinal products, it is advisable for a single and experienced authority to handle all product assessments.

The pharmaceutical industry had proposed to the Commission that the environmental risk assessment for GMO-containing pharmaceuticals should be incorporated into the safety section of the product registration dossier.

Implementation of this suggestion would be a major step towards the "verticalisation" of the regulation. What is required above all is consistency and cohesiveness in the regulations, the effective interaction between horizontal and vertical laws and authorisation procedures, thereby complying with the "one door, one key" principle advocated by the Commission.

The proposals above apply to the marketing of products containing GMOs. There are however requirements of the EC Directives and thus the UK regulations which precede the stage of marketing.

Although there are no immediate proposals for pharmaceutical products containing GMOs to be placed on the market, the Association has concerns over the potential implications for the conduct of clinical trials on such products in the UK. It is understood that the Department of the Environment has accepted that the Department of Health has a primary role in the assessment of medicines containing GMOs at the marketing authorisation stage. At the clinical trial stage it is not evident that the Department of the Environment has conceded the same authority to the Department of Health. It would be an unnecessary duplication and burden upon industry to have to report both to the Department of the Environment and to the Department of Health. The Association would like to see this situation rationalised before duplicate notification and authorisation procedures are established in the Department of the Environment.

Where the process technology, or the early research and development stages, are not already covered by vertical legislation then it is appropriate that they should be regulated under appropriate horizontal legislation. This type of regulation has been in place for many years under, for example, the Health and Safety at Work Act. For contained use aspects there is much doubt within the pharmaceutical industry as to whether additional specific GMO regulations were in fact needed.

8. *How do current regulations compare with those of other competitor countries?*

— In Europe
— In the Far East
— The USA

We note that the Select Committee has previously been advised at length on this matter by the HSE and the Department of the Environment.

The EC Directives on the contained use of genetically modified organisms (90/219/EEC) and on the deliberate release of genetically modified organisms (90/220/EEC) should have been implemented into the national law of Member States by October 1991. To date a number still have to do this. Of those that have implemented the Directives some appear to be more restrictive in their approach compared to the UK, particularly in Germany. Member states do appear to be interpreting the Directives somewhat differently, thus illustrating the continuing difficulties of the texts.

Even when all member states have implemented the Directives we suggest that there will still be differences across Europe because of the varying efficiency of the inspection systems in place.

Biotechnology is one of Japan's most advanced technologies. Although the regulatory system is somewhat complicated it is a favourable one with guidance being favoured over regulation. For laboratory scale experiments a comprehensive set of guidelines are available from the Ministry of Education, Science and Culture and the Science and Technology Agency. The uses of biotechnology are regulated by three ministries, with the Ministry of Health and Welfare (MHW) and the Ministry of International Trade and Industry (MITI) being the most relevant to the pharmaceutical industry.

It is understood that guidance issued by MITI and MHW for the industrial applications for rDNA technology are based closely on those of the OECD.

In Japan GMOs can only be used in industrial processes under the appropriate OECD based containment facilities. If micro-organisms are to be released into the environment, a safety evaluation must be carried out under the supervision of MAFF. Recent proposals to move from a guidance based system to one of regulation was opposed by the main government agencies and industry.

In the United States contained use research in the laboratory is controlled through guidelines issued by the National Institute of Health.

Although the procedures may be different the regulatory control procedures for products derived from biotechnology in the EC, Japan and the USA are of similar stringency.

9. *What are the consequences, or likely consequences of the regulatory regime on the competitiveness of the UK industry, in particular as regards:—*

- Research
- Product Development
- Investment
- Location
- Sales and Marketing

Many of the members of the Association operate internationally and give serious consideration to where they should invest in Research and Development and manufacturing. If it was felt that the UK regulatory environment was less favourable than in other countries then companies would certainly consider relocating, although of course other issues would be taken into account. Increased regulation can limit innovation both in industry and academia. The competitive edge of any industry will be influenced by the regulatory regime. The Association is aware that many of its US-based member companies, even if they carry out much of the Research and Development in the UK, are performing their manufacturing elsewhere. There are signs that many companies are also beginning to increase their biotechnology research in the US.

There are some specific areas of concern arising from the GMO regulations to the pharmaceutical industry. Industry is used to dealing with the bureaucracy of regulatory procedures. Will the regulations cause the innovative academic students to relocate? There is still some uncertainty over pilot plant scale working within Research and Development. The UK authorities appear to have taken a pragmatic approach over the 10 litre definition, but the uncertainty over this matter has not inspired much confidence from an investment point of view. The 60 day prior notification requirement for Group 1 Type B activities could lead to delays which for smaller companies carrying out custom synthesis could have major financial implications. Although the UK appears to have also taken on board industry's concerns over aspects of commercial confidentiality relating to GMO work, there are still some concerns as to the need and level of public access to documentation. The marketing of products containing GMOs will be affected if there are delays in the regulatory process as a result of any duplicate approval procedures.

10. *Is there a danger that the present regulatory regime will prevent the exploitation by British industry of research conducted in the UK science base?*

This question raises both the issues of the exploitation of research by UK based companies and the carrying out the research by industry and the public sector base in the UK.

The Association has frequently expressed concern over the inadequate funding of the science base emphasising that it is essential for the maintenance of the infrastructure of the universities and higher education institutions to be adequately supported, and that there should be support for basic long term research. Academia is under increasingly financial constraints and for many universities, having to comply with the requirements of novel regulatory regimes could lead some of them to pull out of such work if the costs proved too prohibitive. It is also more likely that increased regulatory bureaucracy would stimulate the key researchers to move to a more supportive environment.

The pharmaceutical industry is a global industry and will continue to assess carefully where it should put its investment in Research and Development and manufacturing. Many European countries, and certainly the US and Japan are competitive with the UK academic groups in research into various aspects of biotechnology. Although many other factors will be taken into account, the regulatory climate of a country and how it affects research, in both academia and industry, would certainly be taken into account in a company's choice of location.

11. *How best can issues of public acceptance be addressed?*

This is an important and wide-ranging topic which, we suggest could benefit from a separate inquiry under the auspices of the Select Committee. The Association has no monopoly on ideas on how best the issues of public understanding and acceptance of biotechnology should be addressed. We do perceive it as part of the apparent anti-science feeling prevalent in UK society at present. Despite the continuing efforts of a wide range of organisations there does appear to be much ignorance of, concern about, and in some cases aggressive vocal opposition to the use of biotechnology. It is important that this position is addressed as public perception, and the regulatory authorities perception of such public perception could influence the regulatory framework.

A number of issues are clear however. Industry on its own will not be able to influence public acceptance effectively. As the Eurobarometer survey for the EC Commission illustrated in 1991, the public trusts environmentalists far more than it does industry or politicians. It is also clear that it is not relevant when talking to the public to refer to biotechnology as an all-embracing technology. It is important that the public understands specific benefits that can be developed from individual secors of biotechnology. Biotechnology will not be successful if society or the consumer does not find acceptable applications for it. The Eurobarometer survey reported that almost 60 per cent of the British public named the potential treatment of serious diseases as the most important benefit of biotechnology. The Association, but more importantly its member companies, will continue to emphasise what real healthcare advances can be achieved through biotechnology.

The scientific media are often criticised for emphasising negative aspects of biotechnology. This has clearly been the case in a number of recent television programmes. We suggest however that undue media emphasis on so-called "breakthroughs" can also influence public appreciation of the reality of healthcare developments.

The public should be made aware that a regulatory framework does exist for both products and processes and that it can deal with their concern. The agencies concerned should set aside sufficient resources for dealing with issues of public concern and awareness.

Part of the reponsibilities of the Biotechnology Joint Advisory Board (BJAB) and the DTI's Biotechnology and Chemicals Unit are to promote public understanding of biotechnology. There have been some initiatives through COPUS, The British Association, The Science Museum and the National Centre for Biotechnology Education (NCBE) but we suggest that more needs to be done at a government level. The proposed establishment of the new Biotechnology and Biology Research Council may stimulate further activities in this area.

Issues of concern raised by lobby groups and certain non-governmental organisations are not, we suggest, always truly representative of general public concern. Neverthelesss the non-governmental organisations do play an important role and industry must be prepared to have relevant dialogue with them. There are a number of groups who, for different reasons, do not appear to want to see the development of biotechnology at all. Much of the present concern over the patenting of animals and the development of transgenic animals is based on the views of animal activists who are opposed to all forms of animal usage. The biotechnology implications are largely irrelevant. Concerns over the treatment of genetic disorders through gene therapy will be raised by those with strong religious and ethical views which no amount of rational argument about the benefits to human healthcare will influence. These points are made to illustrate that each product sector and each sector of the "public" needs to be addressed differently.

The Association believes that at present the main focus of improving understanding of science and biotechnology in particular should be at the level of schools and colleges across the whole five to 19 year education system. The Association is particularly active in this field through its encouragement of industry science education liaison activities and through its sponsorship of educational resource materials. The Association has a full time education liaison co-ordinator. We recently published two sets of posters on various aspects of the body and healthcare (which went free to every secondary school in the UK) and are at present sponsoring a publication for 16 to 19 year olds on genetics, gene disease and some of the ethical issues involved. In addition, the Association supports AMRIC (Animals in Medicines Research Information Centre) which provides information on request to the general public on all aspects of animal use, including the use of transgenic animals.

12. *What other factors do you consider will play a crucial role in the competitiveness of the UK biotechnology industry?*

From the viewpoint of the pharmaceutical industry there are a number of factors which we believe could play a negative or positive role in the future. These include:

(i) Short-term healthcare cost containment exercises—the Limited List

In an attempt to reduce the amount spent on NHS medicines, the Government plans to extend the Limited List and ban a wide range of currently available treatments, largely on the grounds of cost. As a result current pharmaceutical research projects seeking advances in treatment in areas covered by the new Limited List will be under threat. Future research depends on the income of sales derived from current branded prescription medicines. Banning NHS sales of hundreds of such medicines will have a knock on effect into research on unconquered problems such as AIDS, Alzheimer's Disease, mental illness, cancer and many other ailments.

(ii) Continued uncertainty over intellectual property rights and patents

Member companies of the Association are concerned over a number of issues relating to the patenting of biotechnology-based products. The proposed EC Directive on the legal protection of biotechnological inventions was initiated to ensure that there was harmonisation of the application of patent law throughout the member states. After numerous amendments, as it stands at present the draft Directive will not achieve such harmonisation, and its provisions relating to compulsory licensing, the patenting of parts of the human body, and certain aspects of "farmers privilege" could be detrimental to the competitiveness of European-based industry.

(iii) The UK Science Base

The long term competitiveness of industry in the UK is dependent on the maintenance of the Science Base. The Association continues to be concerned over the erosion of the public sector science base, particularly in the fields of biomedical research. It is essential that the UK maintains its position as a major contributor to the advancement of scientific and technical knowledge. This will help to attract and retain the best scientists and technologists on which the future economic success of the country depends. In addition to the carrying out of fundamental long-term basic biomedical and biological research, it is important that the universities and higher education institutions continue to provide a strong output of highly trained scientists for industry and academia.

It is hoped that the recently published White Paper on science and technology will play a key role in ensuring the competitiveness of the UK. The pharmaceutical industry welcomes the opportunity to work even closer with academia. We welcome the establishment of the proposed 5-10 year rolling "Forward Look" initiative and the benefits for competitiveness that such foresight analysis should bring. The proposed establishment of a Biology/Biotechnology Research Council will certainly give more emphasis to the benefits of biotechnology.

(iv) Support for the start-up companies

The small innovative organisations need to be better financed and given more incentives so that they can develop their discoveries to a stage where full scale clinical development can take place. As others have pointed out in giving evidence to this inquiry the UK-based SMEs are at a clear disadvantage when compared to their counterparts in the USA. The views of the BioIndustries Association on the financial resources required for SMEs, effects of the UK, taxation system, and the Stock Market rules are particularly relevant here.

We note from the White Paper that SMEs have been targeted by the DTI as requiring specific assistance, particularly in the transferring of technology.

Evidence from the Biochemical Society

1. *What is your interest in biotechnology?*

The Biochemical Society is one of the largest learned societies in the life sciences. It has 8,500 members working in research in biochemistry and the molecular life sciences—the scientific disciplines which underpin biotechnology. This response has been prepared by the Society's Industrial Biochemistry and Biotechnology Group.

4. *Which developments in biotechnology raise issues of safety and how should they be addressed?*

Developments in biotechnology raise no new issues of safety. It is important that the issues which have arisen should be addressed against the background of past experience in the industries concerned.

The development of greatest concern relates to the manipulation of the genome, but the regulatory problems are ethical rather than technical. The regulation of the new technology should not be fundamentally different from the regulation of mutation and selection, and these are processes which have a long history in all of the industries which use living organisms as part of their manufacturing process.

5. *Should biotechnology be regulated by an industry specific regime?*

No, there is no reason thy the industry should be singled out, even if it were possible given the pervasive nature of biotechnology.

6. *From a technical point of view, is horizontal regulation better than vertical regulation?*

Both are essential. In general, as the molecular weight and complexity of the product falls so the need for horizontal regulation moves towards the vertical. This reflects the nature of the analytical techniques which can be applied to small and large molecules.

7. *Should regulation evolve from a horizontal to a vertical approach in each industrial or environmental application?*

No. It depends both on the nature of the product, and on the industrial application.

A greater understanding of a particular food or beverage, for example, might mean moving towards an even greater dependence on horizontal regulation. The regulatory authorities might reasonably insist that the manufacture should be confined to one or two particular processes, or from one or two particular sources. It would also be desirable to control the source of many of the blood products which are used in human medicine no matter how effective analytical methods became.

The current draft amendments for the COSHH Regulations which will implement the European Directive on Biological Agents require that manufacture with microorganisms should be done with processes in the lowest possible hazard category. In a sense this also amounts to horizontal regulation, even though the necessity for it is not directly related to the product.

10. *Is there a danger that the present regulatory regime will prevent the exploitation by British industry of research conducted in the UK science base.*

Yes. A major problem with current legislation is that it is created prospectively rather than retrospectively. The reasons for this situation were set out in the Robens' Report on which the HASAW Act, 1974, was based. One disadvantage which it has brought is the writing of regulations which are actually in advance of the technology to implement them satisfactorily.

For example the Regulations for the Contained Use of Microorganisms, derived as they are from the OECD Guidelines, contain instructions to "Minimise Release" and "Prevent Release" without defining these terms or providing engineering objectives against which they could realistically be tested. Similarly the meaning of "damage to the environment" in para. 107 of the Environmental Protection Act, 1990, while reasonable at a common sense level, could be open to misinterpretation if the wording were rigorously applied. Most people who have worked with these regulations have a clear enough idea of which is intended, but the lack of definition is a problem.

It may be impossible to prevent the release of microorganisms from a contained process, one can only minimise their release to a very small number, less than some target figure per year of operation. Actual attempts to prevent release have made the equipment and facilities for manufacture at Large Scale Contained Category 2 very expensive. Moreover the belief that to prevent release is a sensible objective has led to some hazardous suggestions for improving containment (eg the views of Chapman on seals, see Warren Spring Laboratory Report LR 746 (BT), Aug. 1989).

If the Regulations remain as sensible guidance, to back up industry's responsibilities under COSHH and the HASAW Act, 1974, then they will be useful working documents until new research allows proper engineering objectives to be written. Unfortunately the quality of some of the draft CEN standards which should underpin the legislation, and clarify its application, is poor. Unless action is taken, perhaps through the BSI, to improve this situation the meaning of the regulations will be further confused. Serious difficulties could then arise when the regulations are implemented as legal documents because it may be impossible to do what is being asked.

Any future UK regulations that are substantially different from those of major trading partners will act as non-tariff trade barriers, hindering both the abilities of UK companies to compete and the exploitation of UK R & D strengths.

11. *How can issues of public acceptance be addressed?*

There is an urgent need for a concerted campaign to explain to the public that absolute safety is a chimera. A balance has to be struck between the benefits from technological and scientific advance and the risks that are inherent in the acceptance of the processes which bring those benefits. A public which can properly assess that balance is in a position to decide whether to accept the new processes and the benefits which arise, or to reject them.

It is a sad reflection of the state of the debate in Britain that it is far easier for the teachers in our schools to obtain information which attacks modern technology than it is to find good teaching material which sets out the benefits which have accrued from it. Moreover in a social climate which places financial gain and profit on a par with, if not above, social need, it is inevitable that the ethical debate will question the motives behind the introduction of new technologies.

12. *What other factors do you consider will play a crucial role in the competitiveness of the UK biotechnology industry.*

The industry thrives at the interface between biology, chemistry and engineering. Everything possible should be done to ensure that the interface remains healthy. If new regulations are to be formulated, the costs of their implementation should be borne in mind as many biotechnology companies are small and medium sized and would be unable to bear high implementation costs.

Supplementary evidence from the BioIndustry Association

QUESTION 20—*What is the BIA doing to address the issue of public acceptance?*

The BIA is promoting the public awareness of biotechnology through the following initiatives:

Public Awareness and Information Working Party

This group aims to redress a perceptibly negative bias in general reporting and ensure that the public debate on biotechnology is based on accurate information. The working party is responsible for co-ordinating much of the public awareness activity of the BIA.

Roundtable Meetings

The BIA "animal roundtable" and "crops and food roundtable" meetings are held in conjunction with the Farm and Food Society to discuss the issues surrounding these areas. Participants are from industry and non-governmental organisations, including:

- RSPCA
- Earthkind
- Compassion in World Farming
- Genetics Forum
- Henry Doubleday Research
- Farmers World Network
- Farmers Link
- National Farmers' Union
- Greenpeace
- Green Alliance
- COBAF

BIA Annual Meetings

The first Annual Meeting "Biotechnology—Friend or Foe?" was held in November 1992. It covered the social, ethical, political, religious and economic impacts of biotechnology and was attended by over 230 people, including 30 members of government departments and representatives from over 15 pressure groups. The meeting was addressed by William Waldegrave, Minister for Science and Technology, and firmly placed the BIA and biotechnology at the top of the science agenda in the UK. The programme for the meeting included:

- The Benefits of Biotechnology to Medicine
  Sir David Weatherall, John Radcliffe Hospital, Oxford
- Ethical Restraints on Biotechnological Inventiveness
  Dr John Habgood, Archbishop of York
- Biotechnology: Economics before Ecologics
  Hon Jonathon Porritt
- The Benefits of Biotechnology to Agriculture and Other Biotechnology Based Industries
  Prof Tom Blundell, Director General of the AFRC

Around 15 media representatives also attended and the meeting received a fair amount of press coverage. The second Annual Meeting will be held in November 1993 on the subject of "human genetic research". The BIA has applied for a grant from COPUS (Committee on the Public Understanding of Science) to assist with the funding of this year's event.

International Roundtable

This was a 2-day event held in November 1992 to which Executive Directors from 45 biotechnology trade associations around the world were invited to discuss common issues and exchange information. Those associations invited included:

— ASSOBIOTEC	Italy	— IBAC	Canada
— FBID	Denmark	— IBASA	South Africa
— VCI	Germany	— NZBA	New Zealand
— ORGANIBIO	France	— ABA	Australia
— BBA	Belgium	— JBA	Japan
— ABC, IBA, IBSA	USA		

Two of the workshop sessions were dedicated to public awareness and manpower, education and training.

European Federation of Biotechnology (EFB) Task Group on Public Perceptions of Biotechnology

The BIA is a member of the above EFB Task Group, which aims to foster greater public awareness and understanding of biotechnology and to encourage informed debate about it by developing and implementing appropriate strategies. The Task Group comprises around 40 members from 16 different European countries.

UK Interest Group on Education in Biotechnology

The BIA is represented on the above group which works on educational issues at the national level through the British Co-ordinating Committee on Biotechnology (BCCB) and Europe-wide through the EFB Working Party. The group organises an annual conference as part of the British Association annual science festival. Topics have included:

— "Biotechnology—A New Lifestyle"	1990
— "Biotechnology in Action	1991
— "Biotechnology in the home—an unseen revolution"	1992

The 1993 conference will be "Environmental biotechnology—your neighbourhood watch". This group also co-ordinates Project BEMET (Biotechnology in Europe, Manpower, Education and Training) which aims to facilitate information flow between academia and the European Biotechnology Industry.

Careers Leaflet

The BIA supplies careers and general information to schools etc, when it is requested. The Manpower, Education and Training working party has produced a careers leaflet, sponsored by SERC, which will be distributed to all secondary schools in the UK and at careers fairs etc.

CIA/ABPI/BIA Biotechnology in Europe Exhibition

The BIA occasionally works with other trade associations and lobbying groups in the staging of events. In February 1992 the BIA, along with the Chemical Industries Association (CIA) and the Association of the British Pharmaceutical Industry (ABPI), was involved in the organisation of the "Biotechnology in Europe Exhibition". Attendees had the opportunity to put questions to representatives of the biotechnology community on biotechnology's contribution to the nation's prosperity, economic development, environmental care and individual welfare.

Other Exhibitions

The BIA attends a number of trade fairs and exhibitions throughout the world each year. In August 1992 the BIA had a stand at BIO JAPAN '92, an event held in Tokyo and arranged by the Japan Bioindustry Association to raise the public awareness and understanding of biotechnology.

Lectures

The BIA is occasionally involved in giving one-off lectures, for example a talk entitled "Biotechnology—a place in society?" was recently given to social science students at Nottingham University. The BIA has also recommended speakers for lectures given at Women's Federation meetings around the country.

European Secretariat of National Bioindustry Associations (ESNBA)

The BIA is a founder member of the ESNBA which has as its parent bodies the national bioindustry associations of Belgium, Denmark, France, Italy, Spain, The Netherlands and the UK. One of the main aims of the ESNBA is to provide a European focus for the collation and dissemination of information on national and European issues.

Media Contact

The BIA has a great deal of regular contact with the media, is quoted in several media directories as a source of information, and has a good working relationship with journalists from a number of national newspapers and science journals. The BIA has carried out PR activity to counteract hostile television and press coverage and is also pro-active in a number of ways. It has been involved in the production of a number of videos including one for the Central Office of Information and another for the DTI. The BIA is a regular contributor to several journals including "Biotechnology Bulletin" and "Genetic Engineering News".

Press Releases

The BIA distributes news releases to advise the press of important events and developments. Releases over the past six months have included:

- Biotechnology—friend or foe?
  10 November 1993

- Biotechnologists push at green door
  11 November 1993
- UK sets the stage for international biotechnology co-operation—first international roundtable for bioindustry associations to be held in London
  13 November 1993
- White paper on science and technology—BIA views on the issues to be addressed
  1 December 1993
- UK biotech set to tap financial markets
  2 December 1993
- BIA welcomes London Stock Exchange's proposed rule changes
  14 February 1993
- UK biotechnology into North America
  4 March 1993
- BIA to act as secretariat for UK biotechnology standards committee
  19 March 1993

Position Papers

The BIA prepares and distributes position papers on key issues. Recently, position papers have been produced on:

- The London Stock Exchange's proposed rule changes
- Views on the issues to be addressed in the forthcoming white paper on science and technology
- Genetically modified foods

Supplementary Evidence from the British Bio-technology Group PLC

INTELLECTUAL PROPERTY RIGHTS

1. *Introduction*

This document is a supplement to the submission made by British Biotechnology Group plc on "Regulation of the UK Biotechnology Industry and Global Competitiveness", as requested by the Committee at the Oral Hearing on the 15 April 1993.

It was indicated in the original submission to the Select Committee that the resolution of current problems in biotechnology patents and their interpretation are likely to be critical to the future competitiveness of the UK biotechnology industry. As the biotechnology industry evolves, it is essential for UK industry that good patent protection is obtained on an international level. The aim of this document will be to discuss why patenting is so important to biotechnology, analyse the differences between the major patenting terroritories and examine how these differences could impact on the UK's competitiveness with the rest of the world. Some additional comments on the role of intellectual property in the transfer of technology from our universities to industry will also be made.

2. *Why is intellectual property so important to biotechnology?*

The term "intellectual property" generally relates to patents, copyright, trade marks, registered designs, design rights and trade secrets, the first four being monopolistic and quasi-monopolostic rights, the last a doctrine of practicality, reinforced by contract law and equity. In the context of biotechnology, patenting is probably the most important for a number of reasons, especially since copyright is unlikely to apply to amino acid and nucleotide sequences. First, a granted patent will protect an invention for up to twenty years in the United Kingdom and Europe, and for similar lengths of time in other parts of the world. This period of exclusivity allows the patentee to prevent third parties from practicising the invention without rewarding the patentee, and provides some security to the substantial investment in research and development. Second, because biotechnology is a high-risk, research driven activity, patents often constitute an essential component in the process of technology transfer, particularly from universities to industry. In the early stages of technology transfer, whether it be by a licence arrangement or by setting up a new company to which the patent is assigned, one of the key assets for investors are the patents. For example, venture capitalists usually seek investments where there are patents and are very reluctant to invest in start-ups where there is little or no chance of obtaining patent protection. The London Stocks Exchange also requires a biotechnology company to have granted patents before allowing it to be fully listed on the Stock Exchange.

Recent disputes within the biotechnology industry have starkly demonstrated the value of patents, such as the Amgen vs Genetics Institute case on erythropoietin (EPO), and the Genentech vs Wellcome case on tPA. In the case of Amgen, worldwide sales of EPO are now approaching $500 million, while the loser Genetics Institute, was subsequently acquired by American Home Products.

3. *Criteria of Patentability*

For an invention to be patentable, it has to satisfy a number of criteria. In Europe there are four basic requirements:

- (i) Novelty: This is the most fundamental requirement of patentability. An invention has to be new to be patentable.
- (ii) Non-obviousness: A further requirement is that an invention is non-obvious i.e. there must be an inventive step.
- (iii) Industrial application: All inventions must be "susceptible of industrial application."
- (iv) Non-patentable inventions: Finally, there are provisions covering non-patentable subject matter, such as plant or animal varities and mere discoveries not harnessed in some technical way.

In summary, a patent cannot be granted for any interesting scientific observation, but, only for an invention which satisfies the above criteria. Consequently, patents usually protect technical innovations arising in a new product or process, or an improvement of an existing product or process in almost any area of technology. The invention need not be complicated or 'high-tech' but it must be something which differs from anything done before (the prior art') and involve at least some level of ingenuity, or inventive step.

In Europe and the UK, the term of a patent is twenty years (subject to certain specific cases where a Supplementary Protection Certificate can be issued) from the date of filing. This period of exclusivity allows the patent owner to prevent third parties from practising the invention without consent (e.g. under licence), but it does not necessarily enable the patent owner to practise his or her invention because there may be other, dominating patents, which block the practice of the invention. This issue of dominating patents is common in biotechnology and will be addressed in more detail below.

4. *Comparison of the Patenting Laws in the Principle Patent Territories*

It is instructive to examine the differences in patent law between the principle patenting territories—Europe, the USA and Japan. In Europe, in parallel to the operations of the national patent offices, a system of "umbrella" filings is in operation, whereby a single application can be filed designating a number of member countries. After publication (18 months after priority date) and full examination by the European Patent Office ("EPO"), the application is granted as a patent by the EPO for the designated countries. The current member states are as follows: Austria, Belgium, Denmark, France, Germany, Greece, Ireland, Italy, Luxembourg, Monaco, Netherlands, Portugal, Spain, Sweden, Switzerland/Liechtenstein and the United Kingdom.

A similar system but more limited system operates on a worldwide basis under the Patent Co-operation Treaty ("PCT"). This is an umbrella filing system, similar to the initial stages of the European system. Examples of territories involved in this system are Australia, Canada, Europe, Finland, Korea, Japan, New Zealand, Norway and the USA. There remain a number of territories eg Taiwan and South Africa, which still operate outside the PCT system. No patents are granted under the PCT; after the initial filing steps, a PCT application fragments into a series of national and regional (eg European) patent applications, which are then pursued in the normal way.

The harmonisation of the filing procedures in a large number of territories has a number of advantages. First, and most important, there is a significant reducation of front end costs which gives the patent applicant and owner important time to review the real strength of the patent before incurring large expense. The total cost of patenting on a worldwide basis can range between £30,000 to £100,000, although these costs are spread over a number of years (often up to ten years). A significant proportion of these costs relate to translation fees, and both the European and PCT systems defer these costs. A second advantage is that both of these systems provide good search reports which gives a well directed survey of the prior literature and can indicate whether or not the application is likely to proceed to grant before a significant financial outlay is made.

Despite these moves towards harmonisation, there still remain substantial differences relating to the scope of patentable subject matter between these territories. Table 1 compares biotechnology patent practice on a range of issues from the prosecution of patent applications through to grant and litigation procedures after grant. Differences in patent prosecution between the three territories arise in a number of areas:

- (i) *Disclosure requirements:* The major difference is the requirement for the disclosure in the USA of the best mode of practising the invention. That requirement is not present in European patent law or the law of many other countries. We would not want any shift to a best mode requirement in European law.
- (ii) *Novelty:* Both Japan and Europe operate on a first to file basis for establishing the date of an invention, while the USA operates a first to invent system. The USA also allows a one year grace period during which a disclosure can be made in the public domain, but which will not jeopardise the future patentability of the invention. This provision primarily favours US residents and academic research institutions where the pressure for rapid publication does not undermine future patentability. In Japan, a disclosure in a learned journal within six months of the filing date will not destroy novelty. Such grace periods as there are in Europe are drastically restricted in scope in comparison to those in the USA and Japan. We believe that there should be a harmonisation

between the USA, Japan and Europe and we would favour a first to file system without any grace period.

(iii) *Claims:* These requirements relate to the types of claims granted (and their final scope) in the patent specification. The principle difference is that in Europe and Japan no method of treatment claims are allowed. A number of countries, especially third world countries, do not allow claims to chemical products and formulations *per se,* but only to processes for making them. Similarly, until very recently, Spain and Portugal only allowed process claims, although the final transition to the enforcement of composition of claims may take time.

(iv) *Prosecution procedures:* In the USA there is a duty of disclosure of all relevant information both good and bad, as well as greater flexibility in prosecuting a range of applications through the filing of "continuation" applications.

(v) *Patent term:* There are a number of differences in the length of term (and its method of calculation), and in the manner of opposing granted patents prior to any possible infringement proceedings. In Europe, there is a period for post-grant opposition, while in the USA a request for re-examination is the only procedure. In Japan, oppositions can be made prior to grant, otherwise after grant the only process is an invalidation trial.

In terms of litigation, there are also differences between the three principle territories. One of the major areas of difference concerns the types of issues considered by the Courts. In the UK and USA both infringement and validity are considered in Courts, whereas in Japan and certain continental European countries (such as Germany and Holland) only infringement is considered in Courts. Since it is usual for an allegation of infringement, to raise questions on validity, the running together of the two issues leads to difficulties. Differences also arise in determining the precise scope of the claims, commonly known as the problem of non-literal infringement and in what constitutes experimental use. Generally speaking, carrying out research on a compound which is covered in a competitor's patent, does not constitute infringement. The distinction of where research finishes and commercial exploitation starts varies from territory to territory. However, there is little decided law in this area, and this makes interpretation difficult, particularly in biotechnology, where it is, in addition, often difficult to interpret the final scope of granted claims.

— There remain substantial differences in the patent laws of Europe, USA and Japan. Even in Europe there are differences in interpretation of patent law between European Patent Office and the UK Patent Office and Courts, particularly over the issue of inventive step.

A recent example was the Genentech tPA case where, in the UK, the patent was revoked after an action by Wellcome, whereas in the European Patent Office, a recent Opposition Division upheld the Genentech patent. The same patent has been upheld in Japan and USA.

These differences in national patenting requirements are also amplified due to the subject matter involved—namely, biological entities and processes, or more specifically proteins, genes, vectors and cell lines. There remains a significant knowledge gap between the science and the law. Many decisions of tribunals seem incomprehensible to scientists, and although Courts can rely on scientific assessors, their use is limited.

5. *Differences between Chemical and Biological Patents and Unevenness of Patent Claims*

— The patenting of biotechnology inventions has been predicated on the assumption that such inventions are similar to chemical patents, and that no new rules or guidelines are required in defining the patentability of biotechnology inventions. This is a position which we agree should be achieved but currently, because of the lack of knowledge, cannot be.

There is now a substantial body of case law for chemical patents concerning the scope of claims in relation to exemplification and the prior art. Decades of chemical patent practice have produced generally accepted conventions concerning the balance to be struck between actual exemplification of an invention and the scope of an allowable claim defining the invention. In addition structure/activity relationships are often more clearly discernable with the small molecules of traditional medicinal chemistry.

Such a corpus of knowledge and practice does not exist in biotechnology yet, and it is likely to be some time before such a knowledge base exists. There remains no clear understanding of the interrelationship between structure and function of biological entities and how the scope of patent claims should reflect the extent of uncertainty. There are also outstanding issues surrounding the patentability of gene sequences for known proteins and, in the USA, the Courts have yet to give a definitive ruling on this question, despite a number of cases in which this issue could have been resolved.

There are several consequences of this uncertainty. First, patents are often filed with broad claims which are in reality unsupported in the specification. Second, there is substantial divergence within national patent offices and between national patent offices relating to the final scope of the granted claims. Until recently, the trend was for broad coverage to be granted in the USA and narrower coverage in the European Office. A good example relates to a patent granted to a US company, Chiron Corporation, on particulate vaccines. The patent, "Hybrid Particle Immunogens" discloses the use of hepatitis B surface antigen, which is a particulate protein, fused to a surface glycoprotein derived from the herpes virus (glycoprotein gD). The granted US patent (US 4,722,840) has a very broad claim 1, which reads as follows:

> "A hybrid polypeptide comprising an assembled particle, said hybrid polypeptide comprised of a particle-forming fragment of a structural protein from a virus particle fused to a heterologous amino acid sequence defining an epitopic site of a pathogen or toxin, said heterologous amino acid sequence being disposed within said assembled particle such that said epitopic site is immunologically reactive."

The scope of this claim relates to all particles of viral origin, whereas the European patent, (EP-B-175261), has a much narrower claim 1, relating only to particles based on hepatitis B.

> "A novel hybrid polypeptide comprising a particle forming fragment of the Hepatitis B surface antigen fused to a heterologous amino acid sequence comprising an epitope of a pathogen or toxin."

There are many other examples of patents with variable claim scope. The situation has become more complex recently, in that this trend appears to be reversing, with the US Patent & Trade Marks Office being much stricter on the question of claim scope, than the European Patent Office.

— This variation in the scope of granted claims means that there is an uneven distribution of patent protection in the principal patenting territories of the world.

Added to this, there is the historical perspective of early patents having very broad claims which have been rapidly outstripped by the pace of scientific progress, yet which remain in force. Similar problems exist for natural and second generation modified molecules, where minor structural alterations can give a substantial functional advantage. A good example here is tPA, which is currently marketed by the US company Genentech. Patents granted in Europe (other than in the UK), the USA and Japan are of sufficiently broad scope to preclude any second generation, improved tPA molecules from being marketed without a licence from the original patent owner of tPA. Yet, at the time that the original patent was granted to Genentech, there was no consideration of generating substantially improved molecules. A complicating factor is that compulsory licenses under a dominating patent are easier to obtain in some jurisdictions than others, and in some countries (such as the USA) they are not available at all. If a comparison were made directly with chemical patents, then these second generation molecules, which have significantly improved functional properties over the wild-type, would be independently patentable over the art, and (except in the comparatively rare case of so-called "selection inventions") would not be dominated by earlier applications.

This situation has not been improved by the recent trends in opposition hearings at the European Patent Office. Two recent hearings, one involving the Genentech tPA patent, and the other Amgen's Erythropoietin patent, have both gone in favour of the wide interpretations of Genentech and Amgen, despite strong opposition cases. Although appeals have been lodged against these decisions by a number of companies, the likely result is that each patent, to reduce the breadth of its scope, will have to be opposed again in the various national courts, which will be both time-consuming and costly, as well as highlighting inconsistencies between European and national laws.

There is also an inconsistency in what issues can be raised during examination and during opposition. Prior to granting a patent, the examiner can and should check whether the scope of the proposed claims are supported by the description in the patent specification (Article 84 of the European Patent Convention). **Once a patent has been granted, however, it is impossible to raise this issue of adequate support in opposition.** In contrast, other standard criteria of patentability, such as inventiveness and obviousness can be raised in opposition, as can the issue of whether a patent specification adequately describes the invention clearly and completely enough to put it in the hands of the public.

6. *Intellectual property issues between University and Industry*

Despite the universally acknowledged importance of the role of technology transfer, the commercialisation of inventions by academic scientists and government scientists has been controversial in both the UK and the US for many years. In the US the Bayh-Dole (1980) Act set out procedures for the handling and commercialisation of intellectual property and the methods by which technology could be transferred from universities and government institutions to industry. Crucially, the act specifies that inventors must share in the proceeds and that universities are not permitted to give away patent rights but are entitled to licence them.

In the UK, the removal of the exclusive rights of the then NRDC (now the British Technology Group) in commercialising university inventions has led to a more devolved system where universities take direct responsibility for handling the transfer of their own technology to industry. While this devolution of responsibility is strongly favoured by industry, there remains a substantial gulf between the US and the UK in the success rate of the commercialisation of academic research.

— Technology transfer as it is practised in many universities in the UK is of a highly variable nature.

All too often high class research remains within our universities with little or no chance of being commercialised. A number of universities, such as Oxford, Imperial College and University College London, which have established an excellent reputation for technology transfer, but there are still many centres of academic excellence which lag behind. If inventions are not commercialised, then everyone loses out—not just the investors, but also the universities, industry and the research base.

Technology transfer is a percentage game (the percentage varies from one discipline to another), where for every success story, there are a series of failures.

Consequently, technology transfer, if it is to obtain a satisfactory return, requires adequate financial resourcing and management expertise. Success stories in the US, such as Stanford University, which had a 1992 licensing income in excess of $13 million, and MIT ($6.5 million licensed income) have resulted from the development of sound strategies for technology transfer and the realisation that the pay off historically is very long and financial returns of any magnitude may only occur ten years after patenting.

Over the above issues currently surrounding biotechnology patents described above, there are also complex requirements surrounding the "seeding" of these patents into industry. When it comes to the search for an industrial partner, many universities fail to invest the time and money required for successful technology transfer. There are a number of reasons for this failure:

— The failure to identify a market for the product or technology. Technology transfer has to be market driven.

— The variety of ways of partitioning intellectual property rights and ownership between the university and the industrial partner can also present a problem. For example, joint ownership of patent rights between the university and corporate partner adds to the bureaucracy and is unacceptable to the corporate partner who generally wishes to be in control of the situation and will not object to paying a reasonable royalty to the university once the product is commercialised. The commercial partner will accept that the university has ownership of the patents provided that it can rely on the patent being properly and fully prosecuted and defended and a satisfactory commercial position being available and protected. Universities are not usually prepared to undertake such a financial burden.

— Universities, if they are to be involved in technology transfer, need to pay much more attention to patenting and the mechanisms for technology transfer. The costs of patenting are high, and while the full cost need not be met by universities, universities should be prepared to provide realistic budgets for patenting.

— The risks involved in high costs of patenting can be reduced by careful preparation and ground work. Undertaking literature searches, including patents, prior to filling will at least give an indication of what the competition is doing.

— More importantly, when patents are for biotechnological inventions, universities should, for instance, use patent agents who are expert in this field. there is a substantial difference between engineering inventions and biotechnology inventions, and requiring a patent agent experienced in the one, to draft sound claims for the other is asking too much. In particular, UK universities should enlist patent agents who have had experience of patent filing and prosecution in the US where the rules and tactics vary considerably from the UK.

— Once the patent application has been filed, universities must be prepared to invest the time and effort required to prosecute their applications. For example, interviews with patent examiners, who may be prepared to invest significant time in speaking to academic patent applicants, can help the prosecution process.

— It is also common in academic circles for a patent application to be filed at the last moment prior to publication, not a practice usually followed by commercial organisations. Patent applications filed in a hurry with poor exemplification can jeopardise the future scope of the invention and make prosecution difficult and expensive. Although academic scientists are reluctant to delay publication, more thought about patenting prior to the submission of an article for publication, can save patent problems later on.

For successful technology transfer which is dependent on a strong patent basis, it is essential that universities should focus on protecting the value of their intellectual property rights through the on-going education of academic personnel on patenting and commercialisation options (eg, licensing vs start-up) and through the sensible filing of preliminary patent applications. Furthermore, technology transfer should not be regarded as just another form of university administration. Those responsible in universities for technology transfer should be experienced professionals in this area, who understand the needs of industry. All successful technology transfer offices use technology transfer specialists.

7. *The Human Genome Project*

Problems in different national requirements for patents and their impact on competitiveness has been highlighted by the US National Institutes of Health (NIH) application for 2,000 novel gene sequences, "invented" by Dr Craig Venter, with no known function. Two applications were filed based on "expressed sequence tags" (ESTs), which relate to genes or fragments which have been identified by cDNA sequencing rather than genomic sequencing. The only utility disclosed in the application was that the genes or gene fragments could be used as probes. The ESTs provided no information about the expressed protein, its function or value ie, there was no knowledge of either the complete gene sequences or function in the human body.

The application was initially rejected by the US Patent and Trademarks Office on various grounds including lack of novelty (as the allegedly novel molecules had been claimed very broadly); however, this rejection was only the first stage in the dialogue between the Patent Office Examiner and the applicant.

However, this application and the fact that it was filed by the NIH, has led to a vigorous debate at several different levels. These include general patenting issues:

— The early disclosure of sequences with unknown functions may jeopardise the filing of later patent applications which may contain parts of those sequences but which also define a specified function.

— If a patent is granted for these fragments, then it may dominate later research and could potentially slow down such research, since subsequent research which uses but is not directed at the fragments themselves, might infringe the patent for the fragments.

— Granting patents for sequences without a knowldge of their function, would lead to many companies attempting to patent parts of the genome for themselves, leading to a delay in the development and commercialisation of products.

What appears to be clear is that the patenting of partial sequences of cDNA is not a complete invention but really relates to intermediate research results. The situation should be that until functionality has been defined, there is insufficient data on which to file a patent. The alternative, of issuing such a patent based only on partial sequences, would dominate any late patents filed which ascribed a function to these sequences.

For a company such as British Bio-technology, which often uses biotechnological techniques as a tool to derive small novel chemical compounds, uncertainty over the scope of some patent claims and their relation to experimental use needs clarification. A number of patent applications in the field of adhesion molecules include claims to using antibodies for the screening of compounds. If such claims were to be validly granted, they could slow down research and inhibit commercialisation, because protection would be given for obvious techniques applied to non-obvious subject matter, which is directly analogous to the NIH/Venter application.

At the international level, there are concerns that the NIH's behaviour is an indicator of increasing US protectionism in biotechnology and could inhibit national and international collaboration, including the free exchange of materials. In contrast, in Europe, the European Patent Office last year informed the French minister that it would not grant such an application.

8. *Proposed EC Directive on the Legal Protection of Biotechnological Inventions*

The EC is currently drafting a Directive on the Protection of Biological Inventions. An original draft was proposed in 1988 with the objectives of clarifying the law and providing greater certainty in the Member States, to ensure uniform interpretation throughout the Community and to improve the level of protection for both inventors and investors to the levels available in Japan and the US. This clearly has not happened and in several major respects, the revised proposals are contrary to provisions in the European Patent Convention (EPC), the 1991 International Convention for the Protection of New Varieties of Plants (UPOV), the currently discussed 1991 Dunkel text of the Trade Related aspects of Intellectual Property in the General Agreement on Tariffs and Trade so-called "Uruguay Round" (GATT TRIPS) and the World Intellectual Property Organisation's present negotiations towards a Patent Harmonization Treaty.

More specifically, the draft Directive attempts to address areas such as patenting life forms, particularly animals, and the question of farmer's privileges. The question of patentable subject matter is particularly important in assessing competitiveness with the United States. The recent case of the Harvard "oncomouse" is a case-in-point. The Harvard oncomouse is a transgenic mouse which has a predisposition to forming tumours and can therefore be used as an animal model for assessing anti-tumour agents and thus speeding the progress of a compound to the clinic. Although the application was originally refused by the European Patent Office, it was subsequently granted after an appeal. However, it is currently being opposed by a number of minority interests on ethical and moral grounds. While these groups argue from a moral standpoint, what they fail to realise is that if such life forms were not patentable, then there could be no public disclosure or checks on the use of such modified organisms. Secrecy would therefore be at an even greater premium.

— It is questionable whether the EC needed to draw up such a Directive, and only serves to add another layer of complexity to an already complex situation. What is clear is that European patent law, particularly in relation to the scope of patentable subject matter, will within the field of biotechnology, have to track developments in the US if it is to remain competitive, especially in areas such as the patentability of life forms.

9. *International Harmonisation*

There clearly remains much uncertainty within the field of biotechnology patents, and while parts of this uncertainty will be clarified in the Courts, it is important that harmonization of patent law on a worldwide basis is pursued vigorously.

— The Government should appreciate that moves towards improved harmonisation of patents are urgently needed for the UK to be competitive.

Parallel negotiations are underway through the United Nations' World Intellectual Property Organisation (WIPO) and General Agreements on Tariff and Trade (GATT). The slow rate of progress in these negotiations is disturbing and efforts should be made to speed up the process. It does appear that the US will be moving to a first to file system in 1994, but it is likely that concessions will have to be made in Europe in return.

FIGURE 1

Comparison of Biotechnology Practice EPO/USA/JAPAN

Procecution Topics	*EPO*	*USA*	*JAPAN*
1. Disclosure requirements	Industrial applicability (Arts 52/57 EPC).	Practical utility.	Practical utility.
	No best mode requirement.	Best mode.	No best mode requirement.
2. Novelty	Absolute novelty.	One-year "grace period".	– Modified absolute novelty.
	First to file.	First to invent.	– Six-month grace period provisions.
			– Publicly known or worked *in Japan* destroys novelty.
			– Oral presentation *outside* Japan does not destroy novelty.
			– First to file.
3. Claims			
– 1st medical use	"Compound X for use as an active pharmaceutical substance."	"A pharmaceutical composition for the treatment of Y comprising an effective amount of compound X and a pharmaceutical excipient."	"A composition (or agent) for the treatment of Y comprising as an active ingredient compound X."
– 2nd medical indication	No method of treatment claims, but "use" claims—"use of Compound X for the preparation of a pharmaceutical composition for the treatment of Y".	Method of treatment permitted.	Neither method of treatment nor "use" claim composition—"A composition for the treatment of Y which comprises as an active ingredient compound X".
– Process	Process of analogy is patentable.	Analogous process is not patentable—In re Durden.	Process of analogy is patentable for patentable compound.
4. Biologic Deposits	Available upon appln. publication.	Available upon grant. Restricted availability upon publication of appln.	
	Expert solution.	In re Lundak post-filing deposit.	– Available after grant of any corresponding patent.
5. Prosecution procedures	No duty of disclosure.	CIP/CA aplns.	No duty of disclosure.
		Duty of disclosure.	
6. Post Grant			
– Patent term	20 years after filing.	17 years after grant.	15 years after 2nd publication but no exceed 20 years after filing.
	Post-grant opposition.	Re-examination.	Pre-grant opposition.
			Invalidation trial.

Litigation Topics	*GERMANY*	*USA*	*JAPAN*
1. Warning Letters	Must send warning letter before beginning infringement suit or risk being assessed costs.	Not necessary.	Not necessary.
2. Costs	Loser bears costs of litigation.	Each party bears its own costs, except in "exceptional" case.	Losers bears cost of litigation (not including attorney's fee.)
3. Issues Considered by Court	Infringement only. Revocation (validity) considered in separate forum.	Infringement and validity both considered in court.	Infringement only (validity is determined only in Patent Office.
4. Discovery	Difficult.	Liberal.	Difficult.
5. Preliminary Injunction	Somewhat difficult.	More available.	Available.
6. Doctrine of Equivalents	Covers solutions which the average skilled person can determine vs legal certainty.	Cover "substantially" the same function, way and result.	Some doctrine, based on: —interchangeability; —ease of interchangeability; —equivalents at the time of filing application.
7. Clinical Trials	Are likely infringement if known compound for known indication.	Are not infringement if only for FDA approval.	Are infringement (most likely).

Evidence from the British Veterinary Association

Question 1. *What is your interest in biotechnology?*

The BVA is an organisation established to promote and advance veterinary and allied sciences. It develops its policy in consultation with its membership and numerous external bodies.

The BVA believes that developments in the field of biotechnology provide for significant advances in the treatment and control of disease in all animals, as well as increased agricultural production. The development of new drugs, diagnostic agents and vaccines is welcomed as these will undoubtedly help to ensure better health and welfare.

Question 4. *Which developments in biotechnology raise issues of safety and how should they be addressed?*

Genetic manipulation is the main issue of safety in this area but this is already regulated through the Health and Safety Executive and Department of the Environment with advice from the Advisory Committee on Genetic Manipulation.

If the term "safety" applies to animals as well as human beings, particular effort should be taken to ensure the health and welfare of any animals involved (including any effect on disease and behaviour).

Question 6. *From a technical point of view, is horizontal regulation (where a product is judged through the process by which it is derived) better than vertical regulation (where a product is judged by its characteristics)?*

and Question 7. *Should regulation evolve from a horizontal to a vertical approach in each industrial or environmental application?*

Horizontal and vertical regulation are not mutually exclusive. A product should be judged by its characteristics and not by the process used for its development and production. However horizontal regulation may be appropriate in certain instances.

Question 9. *What are the consequences, or likely consequences, of the regulatory regime on competitiveness of the UK industry, in particular as regards research, product development, investment, location and sales and marketing?*

Unnecessarily severe regulation would without doubt compromise competitiveness in all five areas mentioned.

Policy Statement on Biotechnology

New developments in the field of biotechnology provide for significant advances in the treatment and control of disease in all animals, as well as increased agricultural production. The British Veterinary Association welcomes the development of new drugs, diagnostic agents and vaccines as these will undoubtedly help to ensure better health and welfare. We are most concerned, however, by some of the new and potential developments in the fields of agriculture and medicine, which could have an adverse effect on animals. We want, therefore, to judge each case on its merits.

"Advances" are occurring on many fronts, for example transgenic animals are being developed to improve agricultural production and to produce human medicines such as Factor VIII. The British Veterinary Association's response to a particular case will be based on a critical evaluation of all factors. However, particular note will be taken of the welfare of the animals (including the effect on disease and behaviour), as well as any gain in production that may result directly or indirectly from the genetic manipulations, or from animals being treated with synthetic products. The Association recommends that research should specifically address welfare in such cases.

The production and movement (import/export) of transgenic animals poses a possible problem in that long term adverse effects may not show until later in the animal's life, or only become apparent under certain conditions eg, brought on by transport or production stress. Due consideration will also have to be given to the expected lifetimes of these animals in commercial production. Whilst many, if not all, of these animals will be protected under the Animals (Scientific Procedures) Act 1986 during the experimental stages, we shall be monitoring the situation closely as it develops.

Evidence from Bunting Biological Control Ltd.

EXECUTIVE SUMMARY

The release of beneficial arthropods to suppress crop pests is at the leading edge of environmentally benign technologies that constitute integrated pest management. Natural enemies of pests are collected from nature. Distinct strains with useful characteristics may be sought out or traits heightened by laboratory selection, but no processes of genetic engineering are involved.

Bunting Biological Control Ltd. believe that the use of indigenous species of beneficial arthropods should remain free from government regulation.

The importation and release of non-indigenous beneficials or exotic strains of indigenous species is currently made difficult by controls which require greater clarity.

We recommend the development by an expert working party of clear and simple guidelines for evidence required to prove the environmental safety to the ecology of the UK of non-indigenous or exotic strains of indigenous species.

Standardised criteria and protocols on a global basis, will ensure that the benefits of the technology are available on a wider basis and give access for British companies to export markets.

Detailed comments are set out below directly addressing the questions posed in the Science and Technology Committee Press Notice.

INTEREST IN BIOTECHNOLOGY

Bunting Biological Control Ltd. is the leading UK producer and one of the two leading global suppliers of beneficial arthropods used in biological control systems. These living predators, parasitoid insects and mites are the natural enemies of noxious pests and are used to selectively suppress or eliminate damaging pests in agriculture, horticulture and floriculture.

Additionally, we supply bees for pollination along with expert know how and specialist products for integrated pest management (IPM) in support of prime markets in greenhouse crops and in field vegetables, soft fruits and tree fruits.

IMPORTANCE TO UK INDUSTRY

Integrated Pest Management harnesses all appropriate technologies for the production of healthy, nutritious crops in a cost effective, environmentally sound and sustainable manner. Conventional chemical pesticides are used more selectively or not at all.

Bunting Biological Control Ltd. plays a leading role in the increasing trend to conserve natural resources through IPM helping Britain lead the world in the export of products and techniques to global markets. Consumer demands for healthy food and the avoidance of all non-essential chemical residues has created a premium market for such produce.

THE FUTURE OF THE TECHNOLOGY

The use of beneficial arthropods is aimed at shifting the balance between crop pests and their natural enemies in favour of the latter. Our products are amongst the most natural of all the sciences that make up IPM and have the following long term advantages:

— Give highly cost effective pest management.

— Leave no harmful residues on produce.

— Are safe to users and other agricultural process workers.

— In practical use, the beneficials do not persist beyond the crop cycle.

— Are significantly less expensive to research, develop and introduce.

— Avoid problems of pesticide resistance.

— Are a sustainable resource for long term food and fibre production.

Bunting Biological Control Ltd. believes that consumers, producers, processors, wholesalers and retailers will increasingly demand the short term safety and long term environmental benefits of IPM. We believe that the use of arthropod natural enemies will remain at the leading edge of this demand.

BIOTECHNOLOGY ISSUES

Bunting Biological Control Ltd. do not currently use, nor do we envisage in the future utilising genetic engineering in the development of beneficial arthropods. The organisms we use are usually sourced in the country where use is intended and often in the location or ecological situation of use.

The importation and release of organisms from other countries and other ecological situations poses questions on the consequences of their survival and escape into the natural ecology of the importing country. Regulatory and safety issues revolve around that differentiation. Three classifications should be considered:—

(a) Indigenous species—distinct species specific arthropods naturally occurring in the UK.

(b) Non-indigenous or exotic species collected outside the UK and with no equivalent species found here in nature.

(c) Non-indigenous species or exotic strains of indigenous species where the species *per se* may be found here.

REGULATIONS

The import and export of exotic species or strains of arthropods requires global coordination. There has been an FAO initiative summarised in a report entitled "Expert consultation on guidelines for the introduction of biological control agents"—Rome, Italy 17th September 1991.

Bunting Biological Control Limited agrees with the recommendations of the committee and believes that there should be a government initiative to clarify the situation in the UK and take the lead in standardising global requirements.

We ask that:

> The production and use of indigenous beneficine arthropods in the UK should not be subject to regulations.
>
> The importation of non-indigenous beneficials or identifiable strains of otherwise indigenous beneficials should be regulated as now by the Department of the Environment under the Wildlife and Countryside Act of 1981.

However, we contend that a clear and concise set of guidelines should be developed, by a process of consultation, to establish the evidence required to prove the safety to the UK ecology of proposed introductions. The following should be addressed:—

— Expert identification at species level.

— Tests for best specificity.

— Procedure to eliminate hyper parasites and diseases.

— Pest risk analysis.

— Quarantine procedures.

— Import and export documentation.

COMPARISONS OF REGULATIONS OUTSIDE UK

Governments of Eastern European and developing countries such as China and Brazil have actively supported IPM systems and encourage developments through research funding and few restriction on importation and release.

The USA and Western Europe including the UK all have few, if any, limitations on the use of indigenous species. Their attitude to exotic organisms is poorly defined. Decisions on import and export are left to the discretion of the minister.

The absence of written guidelines discourages applications and complicates the gathering of data. Australia and Canada have producd legislation encouraging initiatives in the field, by clearly and concisely setting out data requirements.

Bunting Biological Control Limited believe that the UK would benefit from a similar system to that in Australia and Canada derived by consultation with experts from government, industry and public interests. Bunting Biological Control Limited would be pleased to assist.

REGULATORY CONSEQUENCES

The enactment of clear and simple regulations covering the importation and use of non-indigenous organisms would greatly encourage Bunting Biological Control Limited to invest further in research and development in the UK for both home and export markets.

CURRENT DANGERS

The current indecisive regulations deter the uptake of research and development projects aimed at the commercial exploitation of non-indigenous beneficials. The British science base is either restricted to working with indigenous species or with exotic species targeted towards aid projects in developing countries, where business prospects for UK industry are not attractive.

The changes recommended by Bunting Biological Control would encourage the wide exploitation of research conducted by the UK science base.

PUBLIC ACCEPTANCE

Beneficial arthropods are seen by the public to be the most natural method of pest management. Their use implies minimal environmental disturbance and is recognised as a desirable component in the production of healthy and nutritious food.

Evidence from the Centre for Exploitation of Science and Technology (CEST), (Dr John Savin)

1. INTRODUCTION

This evidence is based on two projects carried out at CEST from 1991 onwards: (a) Biotechnology as a Competitive Advantage (report supplied); (b) Genomes and Therapy (report in preparation). I have tried to take a realistic look based on economic methods at these technologies and industries. Specifically, the ideas on industry forces and stragetic choice developed in the 1980s by Professor Porter are used. In essence, these state that the health and profitability of an industry sector is determined by the balance of five forces:

- Buyer power (the NHS is a powerful buyer of advanced therapies; farmers are weak buyers of bio-engineered seeds; could the buyer integrate backwards and supply itself?);
- Supplier power (do patents or economies of scale enable suppliers of technology to demand high prices and profits; could the supplier integrate forward into its customer's business?);
- Substitutes (biotechnology is one way of doing something, there can be others);
- New entrants (lots of new companies entering a market tend to reduce profits);
- Rivalry (do the companies have large investments in factories or R&D that need high volumes, how easy financially and psychologically is it to leave the industry).

There are two ways to gain advantage: be a low cost producer or differentiate the products to provide added benefits for the customer. Cost strategies need process innovation. Differentiation needs product innovation and means higher costs but these must be less than the added value seen by the customer.

National competitive advantage is governed by four forces: the skills and cost of people, capital and infrastructure; the presence of globally competitive companies; the presence of globally competitive suppliers (technology, IT, equipment etc); and the match between the home market and global demand (unique home market demand weakens industry as products are not exportable). Government policy and regulation work as external forces on the system. Regulation is assumed to be neutral or that it will encourage upgrading of the industry through higher quality, more acceptable products to consumers and cleaner, leaner, environmentally-friendly production.

The approach looks at these forces in various industries to evaluate changes due to biotechnology. I have grouped the analysis into three industry sectors: agriculture and food, chemical and environmental industries and health.

2. AGRICULTURE AND FOOD

The value chain here is through seeds and animal breeding, farmers, food processors and retailers to consumers.

2.1 *Seeds*

Biotechnology has already reshaped this $20 billion world industry by speeding up breeding programmes, by identifying genes for economically important features and by creating opportunities to engineer crops (antisense technology in tomatoes, adding herbicide resistance and natural pesticides). This coupled with tighter safety and environmental regulation has created scale economics in R&D. Because the industry has consolidated (by acquisition), it has significant supplier power against farmers. New entrants are deterred by high R&D costs and patents. There are substitutes (traditional methods, organic farming, biological crop protection) some of which are also biotechnology based.

Possible future threats lie in the run down of farming subsidies and in retailer and consumer pressures and safety concerns. Further, one-shot pest resistant crops are rapidly overcome by pest evolution, this has been seen already. Companies need economies of marketing to make profits.

Scenarios for this industry are less good than many would like to believe and the emphasis on efficient mass production of basic agricultural commodities is misplaced. Much of the value added by this industry is realised by food processors and retailers. To gain some of this value, seed firms will have to forward integrate to get supplier power with the big food processors. This could be done contractually and through joint ventures with farmers co-operatives.

2.2 *Animal breeding*

Cloning of embryos and transgenic production animals with enhanced characteristics may become big business. It will need high skill levels and economics of scale to work efficently and economically. It also opens the way for rapid disease spread as genetic variety is lost. The comments are similar overall to those for seeds regarding the emphasis on standard animal production units. This industry will add more value by using biotechnology to add to and manage variety. Dutch research shows that the public is generally opposed to exotic (human-animal) transgenic animals in farming.

2.3 *Agriculture*

Advanced agriculture is a high tech solution to a problem which does not exist: food shortage in the developed world. The technologies may be applicable to Developing World crops but there are economic and political substitutes that will be cheaper, faster and more effective (ending of dumping of CAP surpluses on rural African markets for example).

Farming is a low-value added, cost-based business. Agriculture was three per cent of UK GDP in 1984 and this will have further declined. The UK ran a £5 billion deficit in agriculture and food by 1990 with EC countries with similar climates but who are better at marketing. EC farmers are generally not competitive in terms of natural resources (sunlight and cheap labour). The Americas, Antipodes, Eastern Europe and Ukraine are all cheaper producers.

Biotechnology could improve cost efficiency but farmers are too fragmented to have bargaining power with global supply companies. Basic unprocessed foods are cheap, value is added in processing, marketing and distribution. Processing firms and retailers have buying power against farmers. It is difficult for farmers to leave the land increasing rivalry and decreasing prices.

Biotechnology can make farming cleaner and environmentally friendly: both increasingly important and often done only due to government pressure and legislation. Why spend money cleaning water of nitrates and agrochemicals that need not be there anyway? Pesticides traces in food products are monitored so efficient use of the best technology is imperative and saves money overall.

2.4 *Food processing and retailing*

Biotechnology helps improve process efficiency and provides consistent quality. Standardised raw material helps and some farm products can be improved, for example, higher solids in tomatoes. Biotechnology here is generic: companies buy in the best technology. Most government R&D supports increasing agricultural output and not processing efficiency (too near market).

This sector is important to the UK accounting for seven per cent of GDP in 1984 with £33 billion of output. The UK is competitive in whisky and biscuits. Food processors can and do buy globally, they want high-quality standardised raw materials and they have significant buying power. Some are becoming backward integrated to ensure quality and to deploy biotechnology engineered plants and animals as a proprietary advantage (eg Unilever in palm oil). If everyone has the technology, it confers no additional value.

Processors are under pressure in the UK from the big retailers who are bad at developing good supplier relationships: retailers see themselves as traders (the exception is Marks and Spencer). Retail in the rest of the EC is more fragmented with pressure from discount retailers, now coming into the UK. In the USA, FMCG brands have been eroded by price competition with "own brand" goods and reductions in TV advertising as the big networks lost share to cable etc. This could easily happen in the UK and EC. When processor margins are squeezed, farmers are compressed.

Processors and retailers have high fixed investment in factories and superstores. Fine if they can be used to capacity but it is easy to add too much capacity. This means that rivalry can be fierce driving down prices and profits in mature markets. If biotechnology creates scale economies it will lead to more mergers. If biotechnology is used flexibly by processors, it could improve product differentiation and profits so long as there is supplier power with regard to the retailers (who are approaching overcapacity).

2.5 *Customers*

We have a stable population and food market. Customers increasingly want variety at reasonable prices. Customers are very risk averse, anything not understood or seen as unethical will be rejected. Genetic labelling will kill the business given current public mistrust. Nutritional labelling requirements are lax already and poorly understood by the public so heavy emphasis on genetic labelling may confuse and alarm without cause. Companies that pursue technology without gaining acceptance of it will fail.

2.6 *Summary*

Biotechnology is seen as a way to increase output in agriculture whereas it needs to be a tool for efficiency and flexibility in food processing and marketing. Most of the technologies are generic but some industries may consolidate and vertically integrate to capture value and develop competitive advantage through proprietary technology, scale economies and bargaining power.

3. CHEMICALS AND ENVIRONMENTAL PROTECTION

Biotechnology enables some food additives, vitamins and speciality chemicals to be made more effectively (or is the only practical production route). Biotechnology is one tool for the production of chiral drugs and is used extensively by pharmaceutical companies in production.

These technologies are generally generic in themselves but they must be used to stay competitive. Some are patented. As generic technologies, they are competitively neutral, unless you do not use them or use the wrong one. It is critical to ensure that the process used has a learning curve and can be developed as fast as alternative technologies. If not, one is left with high investment in uncompetitive processes. If you are better at improving the cost of a generic process than your competitors, you can achieve a sustained cost leadership advantage—until market demand changes.

Biotechnology could substitute for some chemical procedures and meet increasing environmental legislation through cleaner process technology. Treatment plants can be "bolted onto" the waste pipe but, again, these are standard technologies with learning curve implications.

4. HEALTH AND GENOMES

Health offers the greatest scope for high-value products and is the glamorous bit of biotechnology attracting enormous investment: $600 million equity investment in US genetic therapy companies alone in 1991–92. Bio-pharmaceuticals could account for 10 per cent of world drug sales by the end of the 1990s, about $17 billion in today's money compared with actual sales of around $3 billion today. The UK has about 10 per cent of this market, depending on definition, which is a credible performance if not exciting. Bio-pharmaceuticals are still very expensive (£2,200 per treatment) and over 80 per cent are sold in the USA. This is obviously threatened by healthcare reform so improved production technology to reduce cost is important.

Biotechnology in healthcare is a core R&D advantage, new technologies need to be accessed quickly and prevented from diffusing to competitors through secrecy and patents. Production costs are a very small part of value-added (10 per cent). The industry is very fast moving and the UK has missed out on most recent key technologies that will be critical for genetic therapy. Specifically, we are stuck in the antibody era of the early 80s, the latest hot technologies are in genetic therapy delivery systems, in disease gene identification and in the genetics of aging and cell death.

This is a failure on the part of technology transfer in the UK and also a failure of academic institutions to work widely in these areas with adequate resources. Organisations like MRC do an excellent job, they were one of the first into the genome in the late 80s; established the Collaborative Centre and helped set up two companies. However, there are failures in all four national competitive advantage drivers:

- lack of proactive venture capital investment (most recent UK fund raising has tapped the US markets, about $80 million raised) and shortage of experienced entrepreneurial managers and scientists with good business training (perhaps the Open University MBA will help long-term);
- lack of large company investment in UK biotechnology (they have invested in the USA although this is said to be because the quality of opportunities was not high enough in the UK);
- lack of small suppliers of technology (although the industry is now healthier than at any time with a good set of growing firms it is still very small, many UK SMEs have US corporate partners);

- lack of sophisticated home market demand (NHS is a poor market for bio-pharmaceuticals although this may be because their cost does reflect their performance).

This is important because traditional medicinal chemistry has only palliatives for treatment of chronic disease and, given population aging, such diseases will be enormously economically important after 2010. Today's research will take till 2010 to produce good products so the right signals to the industry and academics now will not pay off till then. Does anyone have a long-enough perspective?

The genome projects coupled with advanced IT could change the drug industry by reducing the barrier to entry created by the tremendously high basic research costs. If one can do computer aided drug design and if drug markets fragment according to the genetics and environment of patients, then pharmaceuticals becomes more fluid and profits smaller. This applies whether the genome merely aids understanding of chronic disease opening up new medicinal chemistry approaches or whether the new genetic therapies now in early clinical trials become effective substitutes.

Control of genetic delivery technologies is critical because there may be 100,000 genes, each with 200 variants, but only 5-6 key delivery technologies, all securely patented. Maybe genetic diagnosis and therapy will be rejected on ethical grounds, maybe it will not work. If it does work it will probably be accepted, and that may unpredictably alter the pattern of competitive advantage. The UK has no base in these new technologies although its science base is excellent if weak in genetic therapy.

One can hardly expect to see the NHS thinking in 20 year horizons given the restructuring—and it is not doing so. Yet genetic-based therapy currently offers the only route to major productivity gains in the management of chronic disease and these diseases will swamp health services and community care programmes within 20 years. The Clothier report was excellent but there are fundamental ethical doubts in the medical profession.

In national economic terms, pharmaceuticals account for under 1 per cent of GDP. The UK has not significant diagnostics industry. In corporate terms, the UK is becoming increasingly marginal. The industry operates globally and invests in the best markets world-wide. Excessive buyer pressure in individual countries will lead to a hollowing out of the industry there. Most major European firms have significant US and Japanese market presence and are investing in growing markets like China.

Long-term, if the cutting and commercial edge is genetic therapy, the EC may find its industry hollowed out and relocated. This is not a prediction, it is a scenario for how one possible future may look. One can produce others: the genome project produces vast amounts of useless data, genetic therapy is too expensive, unethical and unreliable, industry consolidates to gain maximum R&D scale and to improve bargaining power with government buyers, major shifts to China and Russia.

Biotechnology and genomes are regarded narrowly as science base issues when they actually have critical implications for how we might manage society in 20 years time. The UK still has opportunities in the following areas:

- Understanding of chronic disease at the genetic-environmental interface, particularly asthma, rheumatoid arthritis, psychiatric disease. The UK has no significant advantages in senility and dementia. There is strength in cancer research, but the lead has passed to the USA.
- Development of gene therapy. Other technologies, antisense, ribozymes, stem cells, have been locked up unless there are significant new discoveries. However, gene therapy is still open although the pace of research is such that this window will close in 2-3 years.
- Development of IT systems and design tools. IT in this area is not funded unless it has a narrow disease focus. Tools for biotechnology can be as lucrative as the actual therapies. The new EC Genome IT centre in Cambridge will boost this potential but can the UK achieve commercial synergies with this institution?

5. Implications for UK National Competitive Advantage and for Government Policy and Regulation

Including chemicals, industries which do or could use biotechnology account for 12 per cent of UK GDP. In some of these sectors, seeds, agriculture, food processing, chemicals and environmental technologies, biotechnology has the potential to generate significant competitive advantages. To do so, it must be used to keep process efficiencies at or better than world bench-mark standards. If biotechnologies are chosen well and used to add variety together with good logistics and distribution, they are a force for the development of a real innovation economy. If not, they can cause industry consolidation with job losses and increased import penetration.

Research, government policy and regulation need to encourage the ethical use of biotechnology in value-added areas and the generation of variety and differentiation. Use of the technology to produce bulk, low-value commodities for marginal economic gain is pointless especially if customers distrust the ethics and safety of the products.

In healthcare, a new information and design based age is starting based on abundant genome data and new molecular understanding of chronic disease and aging. This could trigger a move to increased industry consolidation or a move towards a much more complex and fragmented market needing intelligent use of IT and genetic therapy to manage and maybe cure the chronic, economically important, diseases of age. The UK industry has missed out a stage in technology development and the major firms are globally positioned and relatively mobile. Sending the right signals now should be an important area of policy and regulation but one which is problematic due to the complex changes in the many healthcare systems.

Supplementary letter to the Clerk from the Centre for Exploitation of Science and Technology (CEST), (Dr. John Savin)

I have been contacted by some of the industry associations (ABPI, CIA) on the value of biotechology to the UK as discussed in the Draft CEST report. I would like to clarify the calculation, if this is allowed, as it is not a linear projection or new product market forecast.

In microeconomics at the firm and industry level, biotechnology is crucial and a core technology. Firms that do not use it effectively will be at a competitive disadvantage.

At the macro level, for biotechnology to increase national wealth through new product launches by 1 per cent needs a £5 billion a year new industry. This is currently unrealistic, even the US biotechnology section has not achieved this yet.

The input-output model used to derive the figure is complex. For example, an increase in agricultural output value increases input costs (as a significant part in farm intra sectoral trade) and puts up food processing costs. These can be offset if food processing gets more efficient due to better raw materials, lower energy costs and lower labour costs. If so, then the output of the energy sector falls and unemployment increases. It is not clear given competitive markets that the processed foods can command higher prices.

Likewise, only a proportion of heavy and fine chemical output is affected by biotechnology. Some fine chemical outputs (pesticides, herbicides) are used by agricultural and specialist intermediates by pharmaceuticals. Again, chemicals may gain by energy efficiency so reducing inputs to that sector.

Pharmaceuticals is less than 1 per cent of GDP and is the one sector insulated from other industries and one where high yielding radical new products could be made. Adding 10 per cent by value to their output would add 0.6 per cent to UK GDP on 1984 values.

The 10 per cent adds 0.15 per cent figure is therefore an indication only of the sensitivity of the UK economy to biotechnology. It is not a prediction as such since it is based on a macroeconomic model not on a product/market demand analysis.

Where we have done such product and market forecasts (*The Value of Antibody Engineering to the UK has such a model*), the UK world share is small. We have a small biotechnology sector that will not make a significant macro economic impact until the next century—if then. Most multinationals have their most advanced biotechnology in the USA, Glaxo's antisense development for example.

If you want an electronic copy of the input-output model, please let me know. It is based on a large spreadsheet. I can also print it out for you.

Letter to the Clerk from The Cobb Breeding Company Ltd. (J. Hunnable, Managing Director)

I am enclosing our response to your questionnaire regarding regulation of biotechnology in the UK Industry. These remarks are numbered in the same sequence as the questions in your enquiry.

In poultry breeding, selection and improvements are done within populations of chickens called lines. Normally two lines of chicken are crossed to produce a parent male and two more to produce a parent female. These parents produce broilers for processing and consumption. In addition, breeding companies may produce more than one type of parent of each sex and they will usually maintain several research lines believed to be of value for the future.

1. Cobb is a primary broiler poultry breeding company with international headquarters in Siloam Springs, Arkansas, USA and pedigree breeding operations in Pineville, Missouri, USA and East Hanningfield, Essex UK. We believe that the tools of biotechnology will permit us to accelerate genetic progress in traits of commercial value to the UK poultry industry.

2. Poultry breeders worldwide are following and investing in new selection techniques derived from recent discoveries in biotechnology. To remain competitive the UK must be able to employ these same research methods and to sell improved chickens resulting from them in the UK, as well as elsewhere. These new techniques promise to increase growth rate, lower feed conversion (pounds of feed per pound of gain), increase per cent meat yield, decrease per cent fat, and increase egg production, hatchability and liveability in our lines. In addition, we should be able to extend our product lines by the introduction of new feather colours, feather types, body types and automatically sexable birds.

3. Biotechnology will allow us to introduce valuable genes into already established lines (introgression), to identify more accurately and at an earlier age, genes already present in these lines (aid selection), to estimate the amount of genetic variation remaining for future improvement within each line (inbreeding), and to maximise the benefits obtained when crossing each pair of lines to produce parents (heterosis).

4. Much research in poultry biotechnology involves the identification genetic markers associated with (linked to) traits of commercial importance. This research requires only the taking of blood samples and the

running of well established lab procedures and is harmless to the environment. The second area involves the transfer of genes from one chicken line (or another species) to another chicken line. Some regulation is likely needed here because desirable genes could conceivably carry with them undesirable genetic materials or produce undesirable effects (unintended consequences) in the recipient chicken. In addition, modified live viruses of poultry are sometimes used to transfer genes. However, genetic material is being successfully transferred without viral vectors and research in this area is expanding.

5. I believe that biotechnology regulations should take into consideration the unique characteristics of each species with which we work. Poultry and especially chickens are relatively easy to confine and inventory. In addition, the avian egg provides a unique laboratory for this research and this may accelerate applications in birds relative to other species.

6. I believe that horizontal regulation is inevitable. The consumer must ultimately be given the choice to purchase or not to purchase a product that has been genetically engineered. He must be made aware of the processes involved in developing and producing this product. Judging a product on its characteristics forces people to weigh cost and risk versus benefits. Developing an objective method of doing this will be difficult.

7. It seems possible that an application of critical value to peoples survival or to the survival of an industry, might require a vertical approach to regulation. A process for requesting this change in procedure should be available.

8. One assumes that EC countries would ultimately have similar regulations to the UK. In the Far East, to date there are no competitors, however any move to regulate the UK could quickly lead to competitive nil regulated programmes being set up. Most of the UK primary breeders competition is in the USA, where in fact there is a parallel programme for Cobb. It would appear that the development of biotechnology has been more accepted in the USA.

9. Horizontal regulation is likely to delay research and product development by requiring more steps in research. Certainly it will increase the cost of these programmes. Location of facilities engaged in this research will be more difficult in some countries than others, but I suspect it may be more difficult in the UK than in the USA. However, poultry companies (including supermarkets and large fully integrated poultry processing companies) will be unlikely to market these new products if they perceive any risk to their customers at all!

10. Clearly the answer to this question is yes. Our company is very conscious of this as a parallel breeding programme is already operational in the USA, where as mentioned in question 8, the development of biotechnology has been more readily accepted.

11. Agricultural scientists and commercial producers should make their viewpoints known through printed materials distributed by professional organisations to students, educators and government officials at all levels. For example in the USA, the Council for Agricultural Science and Technology (CAST), informs students and educators on issues related to changes in food science and the food industry. Special position papers are written by experts in each area and distributed to congressmen on relevant committees.

12. Of course, investments made by a company in biotechnology should be protected in order to recover the cost of this research. Lack of patent protection could reduce the incentive of businesses to invest in biotechnology research.

The answers to these questions were supplied by Dr J Hardiman—Vice President Research & Development (USA) and Ms J Barnard—Research Director (UK).

Supplementary evidence from the Department of the Environment

Comparative Analysis of US and UK regulations covering Deliberate Release and Marketing of GMOs

1. With reference to the question posed in their Lordships' initial request for written evidence from the Department:

> "6. It is reported that, towards the end of the Bush administration in the United States, the regulatory approach of gentetic manipulation changed from largely horizontal (governing processes) to largely vertical (governing products).
> What were the reasons given for this reported change in approach? Would this place UK industry at a competitive disadvantage? does the UK Government intend to respond to this change?"

The following additional evidence, which contrasts the UK and US approaches to regulation, is submitted for consideration.

General Approach

2. The main difference between the UK and US approaches to control of GMOs is usually quoted as being the difference between "horizontal" (or process-based) and "vertical" (or product-based). However, this is something of a simplification of the reality and does not help in the analysis of advantages and disadvantages of the two systems.

3. In the UK, one set of regulations[1] apply to all GMOs which are released into the environment or are put forward for marketing. Approval via these regulations does not exempt products from then needing separate approval through any regulatory system which controls the particular product. For example, a genetically modified biological pesticide would still need to apply for a consent to market under the Control of Pesticides Regulations. But, if no product-specific legislation exists, then the product could be marketed without further regulatory scrutiny (for example, the introduction of a genetically modified microorganism for the clean up of contaminated land).

4. In the US, a decision was taken in the 1980s not to introduce new legislation but rather to use existing product legislation in a "coordinated framework" to control GMOs. The advantage of this system was that no new legislation was introduced. Amongst the disadvantages were that the regulations used to control GMOs were insufficiently flexible to address the questions the US regulators required to be answered and that there was serious disagreement between regulatory agencies regarding what these questions should be (since each individual case relied on separate interpretation of the existing regulations). Furthermore, the US approach does not allow for a mechanism whereby an "approved product" can drop out of the regulatory system; the UK system does.

5. The difference between the two systems are best illustrated by providing some "worked" examples (genetically modified plants, a genetically modified microorganism intended for pesticidal use and a genetically modified microorganism intended for environmental clean-up). These are provided at annex 1.

6. However, it is important to point out that neither counrty's system is static. Biotechnology is a fast moving technology and both the US and the UK are keeping their regulatory systems under ongoing review.

Changes in the UK and US Systems

(i) UK

7. In the UK, Government policy is to derogate the scrutiny for safety of GMOs to specific product regulation where it is appropriate to do so. Thus, when there is an opportunity to revise product legislation and safety aspects are included, the UK will press for the safety considerations in the GMO regulations to be introduced. The best example of this now is EC Council directive 91/414/EEC which makes provision for a risk assessment of the environmental impact of plant protection product corresponding to that in the GMO Deliberate Release Directive. This means that the safety considerations in the existing GMO regulations will be included (in so far as they are relevant to the product in question) in the pesticide specific regulations and the deliberate release directive will be "disapplied" to such products.

8. Once in place, this directive would mean that, in practice, biological pesticides which were GMOs would go through the same regulatory regime as those which were not GMOs. The only difference would be that a number of additional questions would need to be answered to inform the risk assessment of the GMO. Thus, the move from "horizontal" to "vertical" legislation for the GMO biopesticide would not affect the information requirements needed for adequate risk assessment. The only effect would be on the level of administrative burearcracy involved in the regulatory scrutiny. From the perspective of information requirement, the difference between "horizontal" and "vertical" approaches is largely academic.

9. Other examples where the UK is actively seeking pursuing inclusion of GMO information requirements to specific "product" legislation include the EC Medicinal and Veterinary Products Regulation. It contains a requirement for a similar environmental risk assessment to that in the Deliberate Release Directive and outlines a mechanism for consultation with the competent authorities set up under 90/220. Other proposals for "vertical" legislation are at various stages of negotiation within Europe. Regulations dealing with novel foods and animal feeding stuffs provide for such GMO integrated "vertical" regulation and are at various stages of implementation or negotiation.

(ii) US

10. As far as we are aware, four notable changes in the US approach to regulation took place towards the end of the Bush administration.

11. As experience with GMOs has developed, there have been a number of "interpretive statements" made by US regulatory agencies on the scope of their "vertical" regulations. These have been made necessary as a result of the insufficient flexibility in US product legislation referred to in para 4 above. The US Administrative Procedures Act requires agencies to publish such "interpretive statements" in the Federal Register for public information. The changes proposed to US regulations last year intend to allow the approval of products without having to notify the public on each and every case.

12. The first of the new developments was the publication of a "final policy statement" by the Food and Drugs Agency (FDA) on 29 May 1992 on "foods derived from new plant varieties, including plants derived by DNA techniques" (annex 2). In essence, this set out FDA policy on foods derived from GMOs and proposed a mechanism by which "approved products" could drop out of the scope of regulatory scrutiny. The trigger for the timing of this policy statement was the submission of the first GMO plant intended for food use for an

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[1] Genetically Modified Organisms (Deliberate Release) Regulations, 1992 (S.I. 1992/3280 as amended by S.I. 1993/152)

interpretive ruling by FDA. This was the Calgene "Flavr Savr" tomato. The statement sets out FDA policy on dealing with a narrow range of products within a single sector. Hence, it represents a modification within "vertical" legislation necessitated by a new process. The data requirements to satisfy the regulations are now slightly different for such novel foods.

13. Secondly, USDA published a "proposed rule" in the Federal Register on 8 November 1992. This detailed a new system which would allow certain genetically modified crop plants, with which the US Dept Agriculture (USDA) Animal & Plant Health Inspection Service (APHIS) have had considerable experience, to be released without first obtaining a permit. Instead, a system of prior notification would operate (annex 3).

14. As well as changing the level of regulatory scrutiny in light of experience, the proposed rule detailed a system by which users could petition "for nonregulated status": ie like the FDA policy statement, the proposed rule was intended to introduce a formal mechanism to allow "approved products" to be removed from regulatory scrutiny.

15. The trigger for this development was the same as for the FDA case. USDA had been approached by Calgene for an "interpretive statement" on Flavr Savr. Like the FDA statement, this rule is intended to modify existing "vertical" regulations specifically to differentiate between GMOs and non-GMOs.

16. The third development was the publication on 22 January of a proposed regulation by the Environment Protection Agency (EPA) to require permits for releases of genetically modified micro-organisms used as pesticides in trials less than 10 acres (annex 4). This was passed by the White House Office for Management and Budget Issues during the tenure of the Bush administration.

17. Again, this regulation focuses exclusively on GMOs and seeks to extend existing "vertical" regulation only for organisms derived by this process. There was no specific trigger for these regulations, which have been in train for 18 months, partly due to a "freeze" on new regulations imposed earlier last year by the Bush administration.

18. Finally, US EPA are in the process of drafting new regulations which intend to control specifically the introduction of "plants with pesticidal properties" under regulations derived from the Federal Insecticide, Fungicide and Rodenticide Act. These will be additional to existing US regulation of Genetically Modified Plants currently controlled under the Plant Protection Act.

US State-Specific Regulation

19. Finally, in the US there is a need for separate state—as well as federal approval for the release of GMOs. Some states have statutes in place which "rubber stamp" federal approvals, other states have yet to introduce any legislation. Minnesota and North Carolina have developed their own separate legislation, since they see the Federal system as leaving gaps. In August 1992, a new chapter (Chapter 4420) of the Minnesota State Statutes came into effect. This, together with modifications to Chapter 4410, provides for control of the release of "Genetically Engineered Organisms" (a "horizontal" approach). The scheme includes requirements for the preparation of an "Environmental Impact Statement", review by a Genetic Engineering Advisory Committee, publication of a public notice by the applicant and full administrative cost recovery. Exemptions from the scheme are possible, *ad referendum,* if a compatible Federal permit is held.

Administrative Load Imposed by US/UK Regimes

20. There is no authoritative study of the administrative load reguired in order to achieve product approvals either in the US or the UK. Indeed such a study is likely to be inappropriate until several products have passed through the entire system.

21. However, the present system in the UK appears to be operating well. Since the GMO (Deliberate Release) Regulations, 1992 came into force (1st February 1993) seven consents have been issued by the Secretary of State to carry our R & D releases of GMOs. One of these consents was issued through the UK "streamlined procedures" scheme. The average turnaround time for applications was 59 days. Three further applications are in hand (annex. 5).

22. This compares favourably with figures available for the period October 1991 to January 1993 in which time 21 notifications were received, the average turnaround time being 10 to 11 weeks (during this time, a statutory notification scheme was operated for human health and safety and a voluntary scheme for environmental protection).

23. The assertion that the US system for a plant approval involves "filling in two sides of paper" is pure fallacy. Both the UK and the US systems currently involve multiple notifications for some products. The examples at annex 1 illustrates this for three examples. Nevertheless, both the US and the UK are attempting to rationalise their respective systems. The UK has already moved to "streamlined" administrative procedures for handling the release of some GMOs and is leading in Europe in efforts further to "simplify" the system.

24. In the US, there is recognition that the "coordinated framework" had left gaps: current moves are attempting to provide a viable product clearance system, to simplify administrative procedures for some specific crop plants and to plug legislative gaps where organisms currently are not controlled.

25. Nevertheless, this work is not going on in isolation. Both the US and the UK recognise the necessity to avoid the creation of non-tariff barriers when developing policy in this area and to share the burden of providing safety information. Thus there is ever closer collaboration between the two countries in the OECD and at bilateral talks between the EC and the US.

26. In the OECD in particular, new initiatives coming up through the Environment Directorate of the organisation show particular promise: these seek to identify common information needs and to move towards mutual acceptance of safety data for genetically modified crop plants and for microorganisms used in environmental clean-up.

Conclusions

27. Although starting from different viewpoints, the US and UK regulatory systems for the control of GMOs are fast converging. The issues of concern to each country appear to be the same and the information requirements similar. Both systems require multiple notifications for some products, but the UK system has the advantage that the only additional legislation is centralised in one set of regulations. This paper argues that the UK system is more transparent. Finally, the OECD is set to play an increasingly important role in providing a negotiating forum to move towards an international "level playing field".

ANNEX 1

Worked Examples for US/UK Product Approvals (release stage only)

(I) Genetically Modified Crop Plant (notification)

The hypothetical example is a genetically modified tomato expressing the antisense gene to polygalacturonase (*cf* Flavr Savr). Six crop plants with a limited number of genes can be included in this scheme. Details appear in annex 3.

(a) US:

(i) A two page notification must be submitted to APHIS 30 days in advance of the crop being planted. Nevertheless, USDA must reply to the notification before any work can begin.

(ii) A petition for "non-regulated status", to move outwith the scope of the PPA, is required to be published in the Federal Register if the crop is to be marketed. This rule too is currently undergoing simplification.

(iii) Movement of seed across state boundaries requires prior (30 day) notification. A permit is not required.

(iv) Depending on the state in which the trial is being carried out, separate state permits may be required. In most states, this is a formality or no appropriate state statute exists. In Minnesota and north Carolina, separate consents are required to release GMOs under specific state statutes. This involves submission of a case to an advisory panel, similar to the UK system.

(v) If the tomatoes are to be marketed, approval must be sought from FDA. At present, the US approach to food approval is unclear; Flavr Savr tomatoes are currently testing the system.

(vi) The normal USDA plant varieties approval scheme operates as for any crop plant to be placed on the market.

(b) UK:

(i) Consent is required under the GMO (Deliberate Release) Regulations, 1992. This involves statutory consultation with other European Member States. If the release is for research, such consultation is merely an information exchange; views of other states are not binding on the UK. However, if the release is for marketing, views of other states must be taken account of. If there is disagreement, the issue is resolved by qualified majority voting. In Great Britain, the scheme is operated by DOE, but MAFF, HSE, Scottish Office and Welsh Office also must approve any consent given. In Northern Ireland, a separate but parallel system operates.

(ii) If the work involves the use of an *Agrobacterium vector*, a permit is required under the Plant Health Act. This would normally be obtained at an early stage in the construction of the GMO and is not an issue which is specific to release.

(iii) If the tomato is to be marketed as a food, a submission must be made to the Advisory Committee on Novel Foods and Processes (ACNFP) which would issue guidance in concert with the Food Advisory Committee. This procedure is operated jointly by MAFF and Dept Health.

(iv) Finally, the GMO plant would need to undergo trials for Value for Cultivation and Use and for Distinctness Uniformity and Stability as is the case for all crop plants. This procedure is operated by MAFF.

(II) Genetically Modified Crop Plant (requires permit)

The hypothetical example is a genetically modified oil-seed rape (canola) expressing the *Bacillus thuringiensis* endotoxin gene. The purpose of the modification is to improve resistance to pests.

(a) US

(i) An analysis is required under the National Environment Protection Act (NEPA) which may result in a full Environmental Impact Statement. This requires the provision of extensive background information and is subject to iteration by all regulatory agencies with an interest (USDA, EPA & FDA).

(ii) A permit to release is required under the Federal Plant Pest Act (PPA). This is triggered by the use of a DNA sequence from a plant pest in the construction of the GMO (eg *Agrobacterium* vectors or viral promoters). USDA is the regulatory authority. This procedure has now been simplified (a 30 day notification period now applies) for six crop plants which have no hybridisable wild relatives in the US (see annex 3) although these procedures would not apply to this example.

(iii) A petition for "non-regulated status", to move outwith the scope of the PPA, is required to be published in the Federal Register if the crop is to be marketed.

(iv) Under the coordinated framework, EPA is consulted for its view under the Federal Insecticide Fungicide and Rodenticide Act (FIFRA) regarding any plant with pesticidal activity. This is now being put on a more formal footing (ie one which formalises the voluntary agreement under the coordinated framework) by the introduction later this year of specific regulations made under FIFRA for genetically modified plants.

(v) The movement of seed containing DNA sequences of plant pathogens across state boundaries triggers the Plant Quarantine Act. A separate permit is thus required for such movement (required for multi-state trials or for those where trials are carried out in a different state from the one in which the seed is produced).

(vi) Separate state permits may be required.

(vii) If the rape oil is to be marketed, approval must be sought from FDA.

(viii) The normal USDA plant varieties approval scheme operates as for any crop plant to be placed on the market.

(b) UK

(i) Consent is required under the GMO (Deliberate Release) Regulations 1992.

(ii) If the work involves the use of an *Agrobacterium* vector, a permit is required under the Plant Health Act.

(iii) If the tomato is to be marketed as a food, a submission must be made to the Advisory Committee on Novel Foods and Processes (ACNFP).

(iv) The GMO plant would need to undergo trials for Value for Cultivation and Use and for Distinctness Uniformity and Stability.

(II) Genetically Modified Microorganism (Biopesticide)

The hypothetical example is a phytosphere-competent pseudomonad modified to express the same toxin gene as in the plant example at II.

(a) US

(i) A permit is required from EPA under FIFRA. Specific regulations apply to GMO microorganisms in trials under 10 acres (see annex 4). Separate conditions apply to pesticidal residues remaining on target plants after application. A petition for non-regulated status may thus be required to escape from these second set of regulations made under FIFRA.

(ii) A permit is required under the Plant Quarantine Act to move such organisms across state boundaries.

(iii) An Environmental Impact Statement will be required under NEPA if the product is to be marketed.

(iv) Separate state permits may be required as outlined in (I) (a) (iv) above.

(b) UK

(i) A consent is required under the GMO (Deliberate Release) Regulations 1992 (see (I) (b) (i) above).

(ii) Notification must be made (to MAFF, though DOE, HSE and Health also have an interest) under the Control of Pesticide Regulations. The new EC directive 91/414 intends to derogate measures under the GMO regulations to the control of pesticide regulations. This should result in a single set of regulations covering the release and marketing of pesticides in the near future.

(III) Genetically Modified Microorganism (Bioremediation)

The hypothetical example is a pseudomonad modified to express an enzyme which degrades PCBs.

(a) US

(i) A permit is required under EPA regulations made under the Toxic Substances Control Act.

(ii) If the product is to be marketed, an Environmental Impact Statement is required under NEPA.

(iii) Separate state permits may be required as outlined in (I) (a) (iv) above.

(b) UK

(i) A consent is required under the GMO (Deliberate Release) Regulations 1992.

ANNEX 2

Precis of FDA Final Policy Statement

1. Proposed 29 May 1992: deadline for comments was 27 August 1992.

Scope: "Foods derived from new plant varieties, including plants developed by DNA techniques".

Aims: Intended as statement of policy, not as new regulation.

2. The policy statement set out how FDA proposed to deal with "new methods of genetically modifying plants . . . including recombinant DNA techniques and cell fusion techniques [which] enable developers to make genetic modifications in plants, including some modifications that would not be possible with traditional plant breeding methods".

3. The policy statement was issued to respond to "representatives of the food biotechnology industry [who] have expressed to FDA the need for strong but appropriate oversight by Federal agencies to ensure public confidence in foods produced by the new techniques."

4. The document sets out FDA policy on the regulatory status of the new foods, the scientific issues (including the insertion of genetic material into plants) relevant to the consideration of these, the environmental considerations under NEPA (the National Environmental Protection Act) and mechanisms for co-ordination with EPA.

Comment

5. One of the reasons for the publication of this statement was the submission by Calgene of the Flavr Savr tomato for an FDA "interpretive statement". FDA are still considering the case under their new policy.

6. There has been extensive US public comment on the policy statement, much of which has been adverse. However, under the terms of the US Administrative Procedures Act, FDA is not obliged to respond to this nor to react to it.

7. EPA is in the process of finalising new, additional draft regulations under FIFRA which will require an EPA permit for the release of "plants with pesticidal properties" (although this would not apply to the Flavr Savr case).

ANNEX 3

Precis of USDA Proposed Regulation

1. Federal Register 8 November 1992: Animal and Plant Health Inspection Service, USDA proposed a new rule.

Scope: "Genetically Engineered Organisms and Products".

Aims: (i) "Notification Procedures for the Introduction of Certain Regulated Articles".

2. This part of the proposed rule suggests that those wishing to release "transgenic" varieties of six crop plants which APHIS are familiar with will no longer need permits. Instead, a notification scheme will be introduced.

3. The plants are: soybean, maize, tomato, tobacco, cotton and potato. Provision is made for additions to this list as experience accumulates.

4. The characteristics (ie, genes) which may be introduced to these plants if they are to come within the scope of the new system are restricted. The restrictions are extremely detailed, but in short mean that the most likely genes which would be permitted would be those which would improve the agronomic quality of the plants (eg, antisense, new oils, improved post-harvest characteristics): more controversial characteristics like insect and virus resistance could be included when these are proved to be safe. Plants modified to express human or animal pathogen genes are specifically excluded.

(ii) "Petition for Nonregulated Status".

5. The intention of this part of the new rule is to provide a regulatory mechanism by which approved plant products may exit from the compass of the regulations. The only product which has so far exited the process (Flavr Savr tomato) did so by a special mechanism (USDA "interpretive ruling") which necessitated public consultation *via* the Federal Register.

6. This product is not yet on the market, since it is now subject to FDA scrutiny under their "final policy statement".

Status:

7. The new notification procedures for the six crop species have now been implemented although in a slightly modified form. Prior notification of 30 days is required before plants can be released. This modification was, in part, a reaction to substantial public comment on the original proposal.

ANNEX 4

Precis of EPA Proposed Regulation

1. Published in Federal Register on 22 January 1993, these regulations had been in the pipeline for 18 months, but had been caught by President Bush's moratorium on new regulations and by the White House Office of Management and Budget Review.

Scope: Genetically Modified Microorganisms used as pesticides in trials less than 10 acres area.

Aims: To increase regulatory scrutiny for pesticides derived from GMMs.

2. Existing EPA regulations (under FIFRA) cover all pesticides trialled at more than 10 acres. EPA introduced new scheme to increase scrutiny only for pesticides made from GMMs.

3. Bush administration pushed proposed new regulation through before Clinton administration came into effect. Previously, voluntary scheme has operated in US for these types of organism.

Expect to come into force at the end of this year.

Background

4. Second set of draft proposed regulations (under TSCA) due to be published later this year. These will focus on GMMs used for any purpose which is non-food, non-pesticide and non-medicine.

ANNEX 5

GMO RELEASE AND MARKETING: REPORT ON PROCESSING OF CONSENT APPLICATIONS

PERIOD: FEBRUARY - MAY 1993

Target: turn-round applications within 90 days of receipt (plus 60 days for EC clearance of marketing consent applications)

Applicant:	*Application:*	*Received:*	*Decided:*	*Turn-round (days):*
Dealt with:				
1. Plant Breeding International	Release of potato	01-Feb-93	22-Mar-93	49
2: Horticultural Research International	Release of Pseudomonas	04-Feb-93	29-Mar-93	53
3. Zeneca Ltd.	Release of oilseed rape	16-Feb-93	15-Apr-93	58
4. Nickerson BIOCHEM Ltd.	Release of potato	26-Feb-93	12-May-93	75
5. Advance Technologies (Cambridge) Ltd.	Release of potato	01-Mar-93	26-Apr-93	56
6. Advance Technologies (Cambridge) Ltd.	Release of potato	01-Mar-93	26-Apr-93	56
7. Shell Research Ltd.	Release of Eucalyptus	02-Mar-93	05-May-93	64
In hand:				
8. Rhone Poulenc Agriculture Ltd.	Release of oilseed rape	17-May-93		
9. Rothamsted Experimental Station	Release of Rhizobia	01-Jun-93		

SUMMARY:

	Release	*Market*	*Total*
Applications received:	9	0	9
Applications dealt with:	7	0	7
Average turn-round of applications dealt with:	59 days	0	59 days
Applications in hand:	2	0	2
Backlog against target:	0	0	0

Extract from a letter to the Royal Academy of Engineering from Peter Dunnill, The Advanced Centre for Biochemical Engineering, University College London

1. I am Director of the SERC Interdisciplinary Research Centre for Biochemical Engineering—the discipline which translates the science of biotechnology into safe and efficient bioprocesses.

2. The IRC was established in recognition that biotechnology is one of the most important new industrial technologies, a fact recognised by most governments. The UK has a strong pharmaceutical and fine chemicals industry which biotechnology applies to. The UK is second only to the USA in the number of small biotechnology companies and with a strong biological science base these have a good prospect.

3. Agriculture and hence the food industry will be increasingly affected by biotechnology, specifically by genetic engineering. The capacity to treat toxic wastes will also increase.

4. The principal concern is that increasingly we have the capacity to redesign life using genetic engineering. This is a new capability and care must be taken (I have just funded a chair specifically concerned with safe bioprocessing).

5. There are already specific regulations which cover genetically engineered organisms as well as the broad safety regulations of the process industries.

6. Industry has been very insistent on wanting product regulation and I understand this. However, given that biological products are often not single molecular species, the US Food and Drug Administration regulations—which are the key rules—require a definition of the process. Ideally a product should not have to bear any particular label on the process but nevertheless at a technical level it should be regulated. It is doubtful whether this needs more legislation.

7. As more experience accumulates, especially on genetically engineered systems, it may well be possible to focus on the product. However, any switch should be delayed for some years.

8. With regard to genetic engineering, the regulations in continental Europe tend to be more severe than the UK. In the USA they are becoming more modest and in Japan they seem poorly conscious of the need.

9. The recent Paper on release of genetically engineered organisms was very poorly drafted initially. In its new version it is somewhat better. There is concern that the burden of proof—and its cost—is being transferred to university groups. This is especially serious for process engineering groups concerned with scale-up. (We have spent £8m on a new facility to allow research on genetically engineered organisms and the running costs of contained operation are very high. This does pose problems.)

10. I do not believe the present regime will prevent exploitation.

11. We all have to make a considerable effort to educate the public. This is well recognised by the Research Councils and DTI who coordinate their activities in the Biotechnology Joint Advisory Board.

12. The key lies in building up small ventures (I spent 10 years consulting for Lord Rothschild in what was the largest biotechnology venture fund). What forced us to invest in the USA was a lack in the UK of linkage between good bioscience and good small company management capabilities. This could be changed by the DTI, and I have spoken to Dr Geoff Robinson, but it would require an injection of small company people as advisors.

Evidence from the EC Commission

1. *Is the Commission satisfied with progress toward implementation of Directives 219/1990 and 220/1990 in Member countries?*

Significant progress has been made in the implementation of both Directives throughout the Community, even though this process is not yet fully completed. In the Member States concerned, the process of implementation has been completed both by full legal transposition and by the adoption of the necessary administrative procedures. In some other Member States, while a framework law implementing the Directives has been adopted, not all the detailed adminstrative decrees have been adopted yet. In only three Member States is the implementing legislation still under discussion (Luxembourg, Spain and Greece) and it is expected that the process will be completed within 1993. All Member States have designated Competent Authorities to handle dossiers and implement the necessary measures. Over 125 field test notifications and three product notifications have been received by the Commission under Directive 90/220/EEC from nine Member states.

While the Commission cannot be satisfied until the process of implementation is entirely completed, the situation on implementation can nonetheless be considered as encouraging.

2. *It is reported that European industry retains the view that the Directives need to be modified to ensure industry's competitiveness internationally, particularly with the United States and Japan. Does the Commission agree, and if so, what steps are planned to define possible improvements?*

The competitiveness of Europe's industry (including bio-industries) is dependent on the interplay of a great number of factors such as size of the market, costs of research, testing and marketing, company investment policy, intellectual property protection, financing and tax incentives and also the regulatory framework.

These have been analysed in the Commission's Communication on "Promoting the competitive environment for the Industrial Activities based on biotechnology within the Community" of 19 April 1991. It appears from that Communication that the causal link between the regulatory framework in the EC and industry's competitiveness is a complex issue and one which is not amenable to definite conclusions without extensive and careful analysis. Two obvious approaches to this analysis are: first an evaluation of the regulatory framework and research policy efforts in the US and the EC and, second, an assessment of the competitiveness of modern biotechnology activities of EC-based firms with a view to identifying the key determinants of competitiveness.

Both these evaluations are under way at the initiative of the Biotechnology Coordination Committee (SCC). An interim report on "Regulatory Framework and Research Policy Effort on Biotechnology in the EC and the US" focusing on the deliberate release of plants, micro-organisms and microbial pesticides was issued for comments.

As regards the biotechnology regulatory framework itself, the Commission views it as important to keep legislation under review to reflect rapid developments and technical progress which especially in the fast developing field of biotechnology is evident. In this context, the full use of simplification mechanisms foreseen in Directive 90/220/EEC on the deliberate release of genetically modified organisms (GMOs) is a priority. The Commission is currently preparing in close cooperation with Member States and industry a proposal for a Decision on criteria for simplified procedures for genetically modified plants during the research and development stage.

3. *The Biotechnology Coordinating Committee was initiated to promote cooperation between individual EC Directorates on regulatory and other factors affecting the use of biotechnology in the Community. Is coordination now satisfactory? If not, what needs further to be done?*

The importance of biotechnology stems from the fact that it interfaces with other areas of activity such as the chemical, pharmaceutical, agricultural and food industries, as well as having a bearing on the environment, research and development, ethical issues, health and safety and the protection of consumer's interests.

In view of this, the Commission decided in March 1991 to establish a single high-level body called the Biotechnology Coordination Committee (BCC) with the task of internal coordination in the biotechnology field. This committee is composed of representatives of the services which have a direct interest in biotechnology and it has met 15 times.

The remit of the BCC covers the coordination of all Commission work on biotechnology, the examination of Initiatives and the preparation of Commission decisions, the coordination of the Commission's position and representation in important contacts with outside bodies, the establishment of round table for a comprising representatives of all interested parties and the evaluation of the results of Community biotechnology policy.

In practical terms this has meant, for example, that the BCC has coordinated the Commission Communication to Parliament and the Council "Promoting the Competitive Environment for the Industrial Activities based on Biotechnology within the Community" and the stock-taking note thereafter; coordinated major legislative initiatives in this area including an interim report on the EC/US regulatory framework as attached; coordinated the input from the Commission to the work of international organisations on biotechnology (notably the OECD).

Up to now, the BCC has operated satisfactorily, particularly during the development of a reinforced Commission policy on biotechnology which is in particular consistent with the aims of the Community's other policies. However, the need was felt to deepen the discussion on the regulatory framework and the BCC decided to establish a working group on that area. Sometimes however, substantive discussion of issues of principle could have more usefully occurred at an earlier stage of policy development, and the Commission is presently considering how areas of potential controversy might be brought to the attention of the BCC in a more timely manner.

4. *Does the Commission wish to see "horizontal" process-based regulation replaced by "vertical" product-based regulation wherever practicable?*

The overall aim of Community legislation is to ensure consumers' safety and to permit the protection of human, animal and plant health and of the environment. The Community regulatory framework is composed both of horizontal and vertical legislations.

The Community's "horizontal" legislation relates specifically to the environment and to the protection of workers in the workplace. The "vertical" legislation relates specifically to products, e.g., pharmaceuticals, pesticides, novel foods, . . .

The environmental aspects related to the pre-industrial development of a biotechnological application are in particular assessed under the horizontal framework. In the case of placing a product on the market this assessment is or will be integrated in specific product legislation in order to achieve one notification and one authorisation procedure. If such specific legislation does not exist the directive (90/220/EEC) on deliberate release applies. The Commission believes that this ensures a coherent regulatory approach and, in particular, an efficient and simplified interaction between sectorial and horizontal legislation.

5. *The Commission has entered into discussions with the industry over matters which affect the use of biotechnology. How does the Commission attempt to ensure a balance of views between large and small enterprises in discussion on factors affecting the use of biotechnology?*

The Commission has entered into discussions with a variety of interested parties, including representatives from large and small enterprises. For this purpose, a system of round tables was set up between the BCC and the various interested parties. These round tables comprised general discussions on the Communication on the competitive environment for industrial activities based on biotechnology and on a stock-taking note on progress made. The next round table meeting will be held in September and will focus on the biotechnology regulatory framework. It is felt that through this mechanism, the necessary balance of views will be expressed to the Commission.

6. *What further Directives are being considered which will affect industry's efficiency and competitiveness in the use of biotechnology?*

The Commission is currently implementing the policy commitments taken in the Communication on promoting the competitive environment for the industrial activities based on biotechnology within the Community. Only if necessary, and after thorough case by case examination, in the light of characteristics inherent to specific biotechnological products, the Commission will put forward new biotechnology related legislation. At present, two sectoral legislative proposals namely on pesticides and on seeds are under preparation, which enables the Integration of relevant biotechnological assessment procedures in the case of placing these products on the market.

Evidence from the Farm and Food Society

1. Our interest in biotechnology is in connection with our general concern for agriculture and for the future. One of our Committee members has a special interest, having spent 35 years of his working life in the Pharmaceutical Industry.

2. Genetic engineering and biotechnology represent a completely new science, offering technical and commercial opportunities, but with immense responsibilities.

3. In addition to potential advances in medicine, biotechnology could enhance agricultural production and achieve pest and disease control by varying the genetic make-up of animals or plants. However, research is extremely costly, sometimes astronomically so, and the final consequences unknown. Where the objective is something for which there is no need research can be extremely wasteful. The length of time requred may also mean that an original need has ceased to exist by the time the product is ready for the market. BST is a case in point. There is now no need for it in developed countries, it can be a threat to farmers, its safety for human consumers of milk has not been proved and it can be shown to have adverse effects on animals. In the Third world its cost and dependence on veterinary supervision make it unlikely to succeed in the long term. Interim assessments of the need for biotechnological processes or products are needed.

4. All developments of biotechnology raise issues of safety, particularly when products are now being approved with properties unevaluated and unassessed and with characteristics previously unknown. The 1968 Medicines Act and the new proposed legislation do not cover products of biotechnology, and until such time as adequate safeguards can be established, products to be used in humans and/or animals should be segregated into two groups:

(a) Products to be used for the treatment (eg alleviation control or eradication) of a disease or condition, ie a therapeutic use.

(b) Products to be used for yield enhancement (eg an increase in milk production or leaner meat) where no efficacy is claimed, ie a non-therapeutic use.

Group (a) used in a therapeutic capacity will be administered to a limited number of people (4 per cent) or animals, and therefore should be subjected to the same scrutiny as products licensed as medicines. Group (b) used non-therapeutically, by their nature will be consumed by a large proportion of the population (BST, if licensed in the EC to 360 million people). This population, due to (a) modern bulk-marketing of milk, or (b) no detectable tests being available, has no choice as to whether they consume the item in question. These products will in the main be untested. The Government has already stated on the question of BST that if there were any doubts on its safety (although it has not been tested in humans) it would be "ethically unacceptable to use it in in-vivo trials in man. Coversely in the absence of such doubts there would be no reason to conduct such trials."

Registration of products of biotechnology from 1st January 1992 became the province of Brussels which will lead to much less effective control. The expertise of the ECUMP is not so comprehensive as, for example, that of the VPC in the UK, picked to provide a wide range of interest and knowledge, rather than elected as a national representative. In Brussels decisions can be influenced by the professional lobbyist and no country held responsible. It is well recognised that medicine control in the UK was ahead of any other European country, and it will now be weakened.

No-one knows the outcome of any biotechnological experiments. Pitfalls have already become apparent and are likely to continue. In agriculture the safety aspects mainly concern animals, eg the Beltsville pig, crippled with arthritis, nearly blind and suffering from respiratory disorder, none of which was intended.

5. Biotechnology should certainly not be controlled by an industry specific regime. As more and more pharmaceutical companies have been amalgamated into large international organisations, ethics and morals feature further down their list of priorities. In the past, academic independence has been the cornerstone of scientific debate, but as the Government has shelved its responsibility for financing basic research, and academia has of necessity become more commercially orientated and dependent on funding from industry, it naturally influences:

(a) their choice of subject to be researched;

(b) the scope of their published material and the form it takes;

(c) their freedom to discuss the scientific significance of matter emanating from such research.

6. Both horizontal and vertical regulation are needed, especially where experiments are involved. These may involve animal suffering and the final product may also suffer (of the Beltsville pig mentioned above) and animals genetically engineered for leanness, which suffer from cold. Future generations from genetically engineered animals may also develop unforeseen disabilities.

7. It would be desirable for regulation to evolve from a horizontal to a vertical approach in each industrial or environmental application.

8. European regulations are vastly superior to those of the Far East, but considerably more secretive than the USA, due to industry unnecessarily hiding behind Section 118 of the Medicines Act and the lack of a Freedom of Information Act in the UK.

9. Selection and adequate control to ensure that products of biotechnlogy emanating from the UK are effective, and above all safe, would give the UK industry a great advantage in every respect (1-5). There is so much public disquiet (not only in the UK) that a high standard of ethical control might prove a valuable marketing advantage.

10. There is no danger that the present regulatory regime will prevent the exploitation by British industry of research conducted in the UK science base unless this is looked at only in the short term. Otherwise the whole biotechnology industry will be brought into disrepute. This could happen with BST which:

(1) may well be licensed in the EC, when it is not licensed in its country of origin;

(2) which constitutes an untested (human) product being released on 360 million people with possible adverse effects.

11. Factors which could play an essential role in the competitiveness of the UK biotechnology industry are a Freedom of Information Act and adequate new regulations to control this new science. Attempts to influence public acceptance by biased propaganda or half-truths are unlikely to be successful. It is obvious that the industry is most anxious for favourable public opinion, but that considerable doubts exist in the minds of consumer, farmer and animal welfare groups.

12. We feel that to make competitiveness the leading factor in biotechnology is to court disaster. Where does competitiveness end? The possibilities are so disturbing and the public so rightly alarmed that we consider only strict regulations, with efficient and conscientious monitoring can make biotechnology acceptable. This needs urgent action in view of the rapid developments and huge investment involved.

ANNEX: extracts from a Report by the Advisory Committee on Ethics and Biotechnlogy in Animals, Wageningen, May 1990.

ANNEX (Farm and Food Society)

Extracts from a Report by the Advisory Committee on Ethics and Biotechnology in Animals, Wageningen, May 1990

(On 24th April 1989 the Netherlands Minister of Agriculture, Nature Management and Fisheries installed the Advisory Committee on Ethics and Biotechnology in Animals. The Committee met at least once a month until May 1990).

Earlier the Minister put forward proposals concerning biotechnological actions in animals . . .

(a) to protect animal health;

(b) to protect animal welfare;

(c) on ethical grounds.

The impression could be given that the measures on behalf of animal health and welfare differ from the measures taken on ethical grounds. The Committee is of the opinion that this interpretation would be incorrect, for ethical grounds concern animal health and welfare . . . .

Problems of animal biotechnology from an ethical viewpoint. The Committee believes that the following problem areas are to be dealt with: transgenation, embryo manipulation and the administration of substances obtained as a result of biotechnology, such as growth promoters....

The working area of biotechnology is highly varied and the techniques and procedures are complicated and almost impenetrable to lay persons. That is why it is difficult to make the debate transparent....

One of the aims of recombinant DNA technology is to make new populations with new characteristics, which can, be used for human purposes, good and evil purposes. The unprecedented possibilities, the far-reaching consequences and the risks that can hardly be foreseen raise questions in society about their permissibility.... The transgene animal threatens to become a patentable invention. In addition, there are the concern for and uncertainties of the unintended and unforeseen consequences of such changes. All in all, this leads up to the question of the borders of what is permissible. For some these considerations are a reason for rejecting biotechnology, or certain areas of it, on principle....

The sense of values with regard to animals is shifting, especially the criticism of the use of animals as experimental animals and of livestock housing has resulted in the recognition that animals have a value of their own, or an intrinsic value, besides their instrumental value to man.... The function of the animal for man can be made subordinate to the intrinsic value of the animal.

In particular recombinant DNA technology holds risks for man, animal and the environment. Genetically modified animals that spread in the environment or products of such animals may cause unacceptable risks. These risks may involve diseases and other disorders among animals and man as well as suppression of existing forms of life. This may result in a decrease in genetic variation (gen erosion). Gen erosion can also result from uncontrolled utilisation of plants and animals in nature for biotechnological purposes....

There is fear that the developments of research are not under control or that fundamental values and interests of man, animals and the environment are not taken sufficiently into account.... This fear is not incomprehensible.... Processes of scientific research and the application of research results are difficult to assess and therefore opaque, especially to the general public. The research is often confidential, for scientific, economic or politically competitive reasons, so that there cannot be a public weighing of the pros and cons. Besides, the impression is often given that research is necessary because of international competition; other values do not seem to play a role....

In view of the above the Committee has drawn the following conclusions:

(1) There is a need for transparent information about the working areas of biotechnology and its applications in animal production....

(2) Biotechnology, in particular the "makeability" of new forms of life, the breakdown of species barriers and the loss of genetic variation is widely considered a violation of natural values, which clashes with certain philosopies of life. There is a need to do more justice to the ideological, philosophical and ethical aspects of biotechnology in the debate about the policy to be pursued....

(5) There is a need for democratic control of the development of biotechnology. In view of this control an evaluation of the research and application is necessary....

Problems that have arisen refer to some of the new developments, that is, those implying a break in trend. The Committee considers as such; transgenation, embryo manipulation, ie, embryo clones, the formation of chimeras, the administration of substances obtained by biotechnology, such as growth promoters and the application of genetically modified micro-organisms in, for example, vaccines. In transgenation and embryo manipulation the genome is interfered with and/or there are direct consequences for the population structure. As to the administration of substances obtained by biotechnology and genetically modified micro-organisms, human and animal safety and the socio-economic consequences are at issue....

There is little knowledge available of the side-effects of the technologies and there are no well-tried methods or techniques to anticipate and assess these consequences (risks for animals or health and welfare, and risks for the environment and nature). The lack of knowledge is all the more cogent since irrevocability may play a role in the development....

The Committee started with verifying whether there were principles—basic principles—that could prove the assumption that the animals treated in this report are a subject of moral care and cannot be seen as just "artifacts" or biotechnological material....

The far-reaching consequences of biotechnology for the problem areas mentioned require public nature and effective democratic control.

Evidence from the Genetics Forum

1. *What is your interest in biotechnology?*

The Genetics Forum is an independent public interest group working on many aspects of biotechnology. We aim to educate the public about the issues, and, where necessary, campaign for a socially ethically and environmentally responsible use of the technology. The Genetics Forum was founded in 1989. Since then it has initiated and co-ordinated campaigns on patching of genetically engineered plants and animals (the EC directive), Bovine Somatotropin (BST), the release of genetically engineered organisms (GEOs) into the environment, and on genetically engineered food, amongst others.

2. *How and why is biotechnology important to UK industry*

It is our understanding that it is most important at present in agriculture, food processing, pharmaceutical production and forensic science. It is a powerful technology with a wide range of potential applications, but as yet few products on the market.

3. *What future prospects and opportunities does the technology offer?*

Many claims have been made for the potential usefulness of biotechnology, but as yet these claims have not been borne out. It is of course that biotechnology could be used for environmentally and socially beneficial aims. The Genetics Forum would support such aims, but believes that it is necessary for there to be greater public discussion of and control over the technology for such aims to be realised.

We believe that the first major products of biotechnology in agriculture, namely BST and herbicide tolerant plants are harmful, to animals, farmers and the environment. It is apparent, and widely admitted within the biotechnology industry that claims to lead to a dramatic increase in world food production are unrealistic. We are also concerned about the possible social effects of another major area of biotechnology research, the Human Genome Project. This could lead to an increase in discrimination against people with genetic disease, by employers, insurers, and the public at large, with possibilities for eugenics.

4. *Which developments in biotechnology raise issues of safety and how should they be addressed?*

The developments which raise safety issues are (i) genetic engineering in the laboratory (worker safety) (ii) the release of genetically engineered organisms into the environment, and particular instances thereof, (iii) genetically engineered food (iv) gene therapy (v) some bio-pharmaceuticals.

In general, these issues need to be addressed by publicly accountable and open regulation. In the case of laboratory safety, we believe the current regulatory situation is adequate, although a close watch needs to be kept on such areas as the potential of naked DNA to be transferred to human cells and expressed. A general feature of the situation in other cases is the lack of backround scientific knowledge and experience with genetically engineered organisms with which to judge their safety. For example, the release of GEOs which have taken place to date have been on a small scale, and do not address many of the possible hazards of large scale releases. The Royal Commission on Environmental Pollution, in its 13th report noted that there may be threshold effects, for example with respect to establishment of a GEO in the environment. Most trials of plants have taken place in reproductive isolation and do not tell us anything about the hazards of cross pollination. These and other considerations militate against any relaxation of a case by case and step by step approach to regulation. We are opposed to the exempting of particular classes of genetic engineering or particular crops from regulation, or the granting of blanket or long term licenses for release.

In the case of genetically engineered foods, there have been practical trials on safety, and risk assessments appears to rely on a purely theoretical analysis. Food safety must be ensured through strict regulation involving interdisciplinary scientific expertise. In common with the regulation of GEO releases we believe that both the effectiveness of such regulation and its credibility with the public would be improved by the inclusion of a far greater number of consumer and environmentalist representatives on regulatory committees.

5. *Should biotechnology be regulated by an industry-specific regime?*

We do not understand the question. It is the activities of genetic engineering, the products thereof, and their use which pose potential risks. It is these which should be regulated. Although these activities are carried out mainly by industry, others, particularly universities also carry out such activities, and should be subject to regulation.

6. *From a technical point of view, is horizontal regulation (where a product is judged through the process by which it is derived) better than vertical regulation (where a product is judged by its characteristics)?*

We dispute the description of both horizontal and vertical regulation, and the dichotomy between them. Horizontal regulation (eg EC directive 90/220) *covers* allproducts produced by genetic engineering, but the risk arising, in this case from the release of such procucts into the environment, is *judged* according to their expected characteristics as well as the way that they will be used (released) and under what environmental conditions. Such characteristics will depend on the parent organism, the gene introduced *and* the method of their production, ie. genetic engineering. For example, genetic engineering can introduce mutations into the parent organism; the expression of the introduced gene is not always predictable; etc. We would hope that than any regulator, operating under either a horizontal or vertical regulatory scheme would take all these aspects into account.

As we stated above (response to question 4) there is as yet little experience with GEOs. We do not believe that scientists familiar with eg, chemical pesticides and their environmental risks would necessarily be capable of judging the risks of GEOs. Since it is proposed that regulation under product-specific legislation should occur at the stage of marketing a GEO, ie at the stage where additional risks, due to the large scale nature of the release may be expected, the problem is compounded. No doubt the pesticide regulators will confer with their colleagues with expertise in GEOs, but surely a better and safer result would be obtained by allowing the committee which has overseen field testing to maintain continuity of oversight, in order that, for example questions which may have been of minor importance at the small scale release stage, be re-examined at the marketing stage. We believe that from the point of view of logical consistency, and bureaucratic convenience it would be better for all releases to be regulated under Directive 90/220. We suspect that industry lobbying in favour of vertical legislation is an attempt to relax the stringency of regulation at the very point at which the greatest potential risks are proposed.

7. *Should regulation evolve from a horizontal to a vertical approach?*

We believe we have answered this point above.

8. *How do current regulations compare with those of other competitor countries, in Europe, the Far East and the USA.*

We hope that EC Directives 90/219 and 90/220 will eventually harmonise the situation in Europe. We are not expert enough in the situation in the Far East to comment on this. In the USA, the system is still not fully established, and State and Federal systems may, to some extent, conflict.

9. *What are the consequences, or likely consequences of the regulatory regime on competitiveness of the UK industry, in particular as regards research, product development, investment, location, sales and marketing?*

We are not aware of any significant body of statistical or other evidence on these questions. There is clearly no direct correlation between the regulatory regime, which could explain the discrepancy in numbers of releases between, for example, France and the UK. In the absence of such evidence, the question has become the favourite political football of industry. We do not believe that the information requirements under EC Directive 90/220 are unreasonable or should place a severe burden on any company wishing to carry out a release. We believe that these requirements are essential to ensure safe regulatory decisions, and if this places too severe a burden then either the release is too dangerous or the company incompetent. As many industry representatives have stated, both in private and public, it is not in the interests of industry to take risks with this new technology, especially if a public backlash could result.

10. *Is there a danger that the present regulatory regime will prevent the exploitation by British industry of research carried on in the UK science base?*

We do not believe so. Normally the factor which is cited as likely to lead to such an outcome is a lack of sufficient intellectual property protection. In general, the approach of The Genetics Forum to such questions is that safety comes first. If companies in other countries, through lack of a sufficient regulatory regime have the opportunity to carry out research and release products which would be judged unsafe in the UK, then this can only benefit UK companies, since such foreign companies would undoubtedly suffer as a result of their risky adventures which would not have been permitted in the UK. We assume, that this is the reason that, with certain notorious exceptions, very few releases have been carried out in countries lacking a regulatory regime.

11. *How can issues of public acceptance best be addressed?*

The Genetics Forum does not seek public *acceptance* of biotechnology, but rather that biotechnology be developed in dialogue with the public, and in accordance with the public interest.

Firstly, it is important that industry accept the need for such dialogue, a pre-requisite for which is openness on the part of industry as to what it is doing. In order for industry to gain the trust of the public, which recent opinion polls (the 1991 Eurobarometer) indicates it does not have, it must not attempt to introduce its products by stealth. This will mean that all genetically engineered foods are labelled as such. Secondly, there is a need for a major programme of public education about biotechnology, which addresses the risks as well as the benefits.

12. *What other factors do you consider will play a crucial role in the competitiveness of the UK biotechnology industry.*

We are not sure that the regulatory regime plays a crucial role in competitiveness, so long as it ensures a minimum degree of safety. Other factors most often cited are intellectual property rights and public attitudes, as well as the attitudes of the investment community and the availability of skilled person power.

Evidence from Greenpeace

1. *What is your interest in biotechnology?*

Greenpeace is an environmental organisation formed in 1971 in North America which now has 400,000 supporters in the UK and 4 million worldwide. Greenpeace has no party political allegiances and takes no funds from governments or industry. All our funds come from individual donations making us a truly independent organisation, whose only interest is in the protection of the environment.

Much of the debate surrounding the new biotechnologies, and genetic engineering in particular, has concerned the risks of the release to the environment of genetically manipulated organisms (GMOs). Greenpeace considers genetic engineering to be fundamentally new and different from other, traditional, biotechnologies. It gives the ability to transcend species barriers and thereby change evolutionary pathways. Greenpeace has kept itself informed about the technology, has commented on regulations concerning GMOs in the UK since 1989 and has campaigned internationally on the issue.

Greenpeace is opposed to the release of genetically engineered organisms to the environment because of the dangers that the technology poses. This submission deals with the enviromental importance of the industry in relation to the release of GMOs. It does not deal with wider issues, such as medical use, which are outside the expertise of Greenpeace.

2. *How and why is biotechnology important to UK industry?*

Greenpeace believes that claims for the importance of a potential industry are often overstated and should be examined critically. In many cases there may be alternatives that are environmentally safer. Viewing biotechnology as of overriding importance to the future of UK industry may lead to a complacency in industry which will ignore these alternatives.

3. *What future prospects and opportunities does the technology offer?*

The prospects and opportunities of the technology should also be examined rigorously before claims it will, for instance, "feed the world" are accepted. Often such claims ignore the fundamental political, economic and social factors underlying the problems. There is a temptation to try and escape these problems by escalating technical "fixes". Redefining and restructuring the basis of life is such a technofix frontier.

The claims for genetic engineering benefits, which are purely hypothetical, must be weighed against the risks of the release of GMOs to the environment. These risks have been recognised by scientists and governments and enshrined in policy in an effort to prevent environmental harm. Not all these risks are theoretical. Some, such as the transfer of genes between crops and weedy relatives, have been clearly demonstrated in field trials. The danger of genetic pollution of the environment must be prevented.

If farsighted measures designed to protect the environment are now overturned on the basis of possible commercial benefits, the result may be irreversible. Genetic pollution may not be detached for decades. As such living material can reproduce the danger will be self-replicating and no remediation measures are available. This raises fundamental questions beyond the simple confines of potential commercial advantage.

4. *Which developments in biotechnology raise issues of safety and how should they be addressed?*

The issue of most concern in terms of environmental safety is that of the release of GMOs and genetic pollution. The potential risks of the release of GMOs are detailed in the Royal Commission on Environmental Pollution's 13th report.[1] They include:

(i) the transfer of the "foreign" gene to wild relatives

(ii) the creation of new pests

(iii) the disturbance of ecosystems and natural processes

(iv) the creation of new pests

The case of herbicide resistant plants illustrates these dangers. Crop plants are being engineered to be resistant to normally toxic herbicides.

This will allow the herbicide to be used on new crops and at times when it was not previously possible to do so. Not only will the use of the herbcide increase, but there may be a transfer of the resistance gene to weedy relatives creating a new pest. The increased use of herbicide may also select for the natural emergence of resistant weeds and the crop may itself become a pest especially if it persists as a "volunteer" in the next crop and cannot be killed by the herbicide.

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[1] The Royal Commission on Environmental Pollution: Thirteenth Report: The release of Genetically Engineered Organisms to the Environment. July 1989. HMSO

There is experimental evidence that the transfer of genes from crops to neighbouring plants of both the same and related species does take place.

For instance, gene transfer has been shown between oil seed rape (Brassica napus) and its weedy relative turnip rape (Brassica campestris)[2].

There has been no scientific evidence produced to show that any of the risks of release of GMOs can be discounted. With the possibility of such serious harm to the environment it is vitally important that claims of safety must be rigorously examined. Greenpeace urges the committee to consult truely independent scientific experts on this point.

5. *Should biotechnology be regulated by an industry specific regime?*

Greenpeace does not understand what is meant by "industry specific regime". If this means regulation by process then Greepeace does feel this is appropriate because genetic engineering is a novel technology, bringing with it unprecedented risks to the environment. For a more detailed response see answer to question 6.

6. *From a technical point of view, is horizontal regulation (where a product is judged through the process by which it is derived) better than vertical regulation (where a product is judged by its characteristics)?*

Like many others, Greenpeace is convinced that genetic engineering is a new and "special" case raising an entire new class of risk.

The technology, unlike any other, allows the transfer of genetic material between unrelated species. Claims that it is simply a speeding up of other breeding techniques miss the point. There is no other means by which genetic material could be transferred from a human to a plant or a fish. The concerns over environmental safety relate directly to the way the technology transcends species barriers. The reconstruction of nature is not a trifling technicality to be lightly countenanced.

The dangers and risks of the technology are very different from those of products which may aim to have the same effect but are composed of a totally different material. So, for instance, it is difficult to envisage how a procedure designed to deal with the safety of a chemical pesticide would have the capaciy to deal with the risks and safety issues around a virus genetically designed to kill the same pests. Therefore allowing product assessment alone (vertical regulation) would not deal properly with issues of environmental safety in relation to GMOs.

Greenpeace therefore believes that it is essential that horizontal regulation remains in place.

7. *Should regulation evolve from a horizontal to a vertical approach in each industrial or environmental application?*

Because of the novel nature of genetic engineering, Greenpeace believes this would not be appropriate. Greenpeace believes that the release of GMOs should not be sanctioned under any legislation. However, at the very minimum, features of the current legislation (case by case assessment of each release by a suitably qualified committee, a public register and a consultation period) would have to be enshrined in horizontal legislation.

8. *How do current regulations compare with those in Europe, in the Far East, in the USA?*

Because UK regulations implement EC Directives the approach is broadly similar in all European countries. There are some notable differences however. Denmark takes its public consultation on releases seriously, circulating applications for releases widely to concerned groups or indivduals. In contrast, the UK has no requirement for public consultation and no facility for appeal against a decision of the Secretary of State for the Environment. Finding out about proposed releases in the UK takes a considerable commitment from interested parties even though these are on the public register.

Japan has had very few releases of GMOs but it regulates its gene technology on a process basis.

The USA has moved, with no scientific justification, away from a process, to a product based legislation. It is also a very complicated procedure and must suffer from a lack of overview of the technology.

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[2] Leckie, D., Smithson, A. & Crute, I.R. (1993) Gene movement from oilseed rape to weedy populations—a component of risk assessment for transgenic cultivars. Aspects of Applied Biology 35: 61-66

9. *What are the consequences, or likely consequences of the regulatory regime on competitiveness of the UK industry, in particular as regards: research, product development, investment, location, sales and marketing?*

The current regulations were established after considerable thought and consultation. The Royal Commission on Environmental Pollution proposed such an approach to regulation. The claims that any of these may be adversely impacted by current regulations must be carefully evaluated and supported by verifiable information.

The "needs" of the UK must not be equated with the short term commercial desires needs of section of industry. There is a need to protect the environment of the whole of society.

10. *Is there a danger that the present regulatory regime will prevent the exploitation by British Industry of research conducted in the UK?*

Greenpeace does not believe that there should be encouragement of industry to exploit scientific research which will result in the release of GMOs to the environment. Environmental regulation is designed to protect the environment and if, as a consequence, the exploitation of areas of science which may be damaging to the environment is discouraged this is only right and proper.

There are many other areas of science which may be environmentally safer present other opportunities for industry.

11. *How can the issues of public acceptance be addressed?*

Industry must recognise that the public has a legitimate interest in new technologies. The public has a right to be consulted on such issues and for views to be respected and acted upon. Industry's attitude should not be one of secrecy. It must be willing to consider openly the dangers of the technology and the desirability or otherwise of taking the risks involved.

Greenpeace urges the committee to seek evidence from a wide cross section of society, including public interest groups before forming its views.

12. *What other factors do you consider will play a crucial role in the competitiveness of the UK biotechnology industry?*

There should be an International Agreement on the safety of biotechnology. This would ensure that conditions were similar worldwide and would allow proper consideration of safety issues as risks will not be able to be contained inside national or regional boundaries.

The UK Government should encourage the negotiation of such an International Agreement under the Biodiversity Convention agreed in Rio in 1992.

Evidence from the Japanese Embassy

1. *How important does your Government perceive biotechnology to be?*

In Japan, we recognise that biotechnology is one of the basic technologies for science and industry and has a number of possibilities including the development of new effective drugs and resolution of food and environmental problems.

The five governmental organisations, the Ministry of International Trade and Industries (MITI), Ministry of Health and Welfare (MHW), Ministry of Agriculture, Forestry and Fisheries (MAFF), Science and Technology Agency (STA) and Ministry of Education (ME) practice the promotive policy of biotechnology, while securing safety.

2. *Which developments in biotechnology are thought to raise safety issues?*

It is apparent from the scientific knowledge accumulated over the last 20 years that there have been no specific risk concerning biotechnology safety.

And we think that biotechnology does not give rise to actual problems, but the accumulation of further knowledge and experience is necessary to secure safety for novel application of biotechnology.

3. *In your country, is biotechnology regulated by a specific regulatory regime?*

The safety of products is ensured by laws corresponding to the respective characteristic (medicine, foods, chemicals, etc.) of the products whether the biotechnology is used or not.

As to the industrial use of recombinant technology, Japanese government agencies made their guidelines, as stated below, based mainly on the recommendation of the OECD Council in 1986, which stated that there is no scientific basis for specific legislation of the use of recombinant DNA organism.

(1) Guidelines for Industrial Applications of Recombinant DNA Technology (Ministry of International Trade and Industry 1986)

(2) Guidelines for Manufacture of Drugs Using Recombinant DNA Technolgy (Ministry of Health and Welfare 1986)

(3) Guidelines for the Application of Recombinant DNA Organisms in Agriculture, Forestry, Fisheries, the Food Industry and Other Related Industries (Ministry of Agriculture, Forestry and Fisheries 1989)

(4) Guidelines for Recombinant DNA Experiments (Science and Technology Agency 1979)

(5) Guidelines for Recombinant DNA Experiments in MONBUSHO (Ministry of Education 1979)

(6) Guidelines for Manufacturing Foods and Food Additives by Application of Recombinant DNA Techniques (Ministry of Health and Welfare 1991)

(7) Guidelines for Safety Assessment of Foods and Food Additives Produced by Recombinant DNA Techniques (Ministry of Health and Welfare 1991)

4. *Do regulations distinguish between contained use and general release (for experiment or marketing)?*

YES.

Contained experiments of rDNA organisms are regulated by STA or ME guidelines. Contained applications of rDNA organisms to industrial production process are regulated by MITI, MHW and MAFF.

With respect to environmental application of rDNA organisms, especially rDNA plants, MAFF evaluates their safety on the basis of results of confined experiments conducted under STA and ME guidelines and limited small-scale field tests conducted under MAFF guidelines. These experiments have been conducted, aiming at a preparation for further application in an environment in which appropriate cultural practices will be applied without requiring any specific measures for confinement.

5. *Is regulation in your country "horizontal" (where a product is judged through the process by which it is derived) or "vertical" (where a product is judged by is characteristics)? Which is preferred by your Government?*

We think that there is no scientific basis for specific regulation of biotechnology.

In the guidelines, the safety of biotechnology is ensured corresponding to respective using fields (medicine, foods, industry).

In that respect, we think the guidelines are a "vertical" approach. (See 3 above .)

6. *Is biotechnology publicly accepted in your country?*

YES.

The governmental organisations exchange the information concerning biotechnology with each other and with the general public. We are getting their understanding for biotechnology.

Evidence from Dr Barry Miller: DNA science in schools—A practical approach

1. INTRODUCTION/BACKGROUND

Recombinant DNA technology has secured its position as a major science within the last 10 years or so. It already makes a significant contribution in many fields of direct relevance to the well-being of mankind. Powerful techniques for the investigation, diagnosis and treatment of genetic and other diseases are being developed. Valuable molecules, including rare and exotic pharmaceuticals, are being produced by genetically modified bacteria. The genetic material of crop plants is being modified not only to make them more productive but also to make them resistant to insect attack. DNA fingerprinting is revolutionising investigations into phylogenetic relationships and is being used increasingly in forensic and other legal fields.

2. *Reasons for practical work in DNA in schools*

Not only is the science revolutionising the speed at which our understanding of life processes is being unravelled but it is also forming the basis of an immense industry in terms of employment and wealth generation. The need for a greater public awareness of the technology is self-evident to those in research and in industry who work with the technology. The importance of educating school students about the science so they can take an informed part in the debate on the ethical issues raised by the science cannot be over stressed. Increased literacy of the science within the UK is also necessary if we are to fully exploit the commercial potential available through the science both because of the public awareness factor and also through the provision of young people of the correct calibre entering higher education with a career intention in the science.

Even in the hands of the best teacher a theory-only approach can be dull, dry and repetitive. To spark the science to life requires the inclusion of exciting and challenging hands-on practical work.

3. *Current school position*

All recently revised advanced UK school biology courses and some chemistry courses cover some of the theory behind recombinant DNA technology. There is some discussion of the ethical issues raised by the science, however, the "newness" of the science, together with the assumption that it is too sophisticated, too expensive and too dangerous to pursue in schools has the result that no practical work in the science is included in school curricula.

4. *Science and Plants for Schools approach*

Dr M Barry Miller a seconded teacher working for the Science and Plants for Schools (SAPS) project working with Geraldine Russell and Professor David Ingram in Edinburgh and Richard Price in Cambridge and with the active help and encouragement from very many in research and industry has developed a strategy to introduce practical DNA technology to UK schools. The methods are cheap, safe and reliable and, although challenging, are relatively straightforward. The techniques are carried out with a DNA kit which has been developed by SAPS and with basic equipment already available in schools. The kit contains safe substitutes for the many toxic reagents used in standard DNA research. The kit contains all of the reagents and hardware required for the introduction of the technology to schools. Technical details of the kit, which costs around £35, are given in 9 below. From this costing it can be seen that it is a realistic proposition for schools. Although compromises are made with the kit it would take £4–5,000 of research equipment to allow a similar degree of experimentation to take place. Importantly, there is no real loss in quality using the kit.

5. *Position elsewhere*

Elsewhere major initiatives have taken place. These include programmes in the USA and in Denmark. Both of these programmes make use of expensive research equipment, certain to be beyond the budgets of UK schools. They also use toxic reagents which are banned in UK schools and incorporate plasmid transformations which would be precluded by the complexity of the regulations governing Genetically Modified Organisms.

6. *SAPS funding and future*

SAPS at the Royal Botanic Garden Edinburgh has been funded by a grant of nearly £300,000 over two years from the Gatsby Foundation. Current funding has been offered by Gatsby for a further two year period to allow the work to continue. A further substantial grant has been secured from the Darwin Trust, Edinburgh. Various smaller grants have also been raised. Some central funding would be of great benefit to the work of the project in establishing "official credibility" as well as monies for the work.

Currently the whole project hangs in the balance because Dumfries and Galloway Regional Council, Dr Miller's employer are refusing permission to grant a further period of secondment unless he resigns his post at Stranraer Academy. This effectively means he will return to his post in Stranraer in August 1993, unless this situation can be urgently resolved.

7. *Workshops*

Current workshops for teachers offered by SAPS cover DNA extraction and restriction analysis. Plant DNA is extracted and cut with restriction enzymes and the DNA fragments are separated by horizontal gel electrophoresis. Other DNAs are restricted and analysed by electrophoresis and the band patterns interpreted. Lambda phange DNA is mapped following restriction by a number of different restriction enzymes and electrophoresis. The results of this practical analysis is compared with results predicted from a computer analysis (on a Macintosh PC) of the entire lambda DNA base sequence.

The emphasis in the workshop is to cover techniques which although complex, are practical and can be immediately introduced into UK schools. The techniques are exciting, challenging and provide young people with a thought-provoking insight into the practical aspects of this "secret" science.

Around 180 of Scotland's biology teachers applied for 32 places available in a series of DNA workshops being run in June at the Royal Botanic Garden, Edinburgh. This indicates the very considerable interest and demand for the material on offer. Other recent workshops include one which took place in Cambridge on 11–12 June. To date 70 UK school teachers have attended SAPS DNA technology workshops. If Dr Miller's continued secondment is secured the funding is in place to deliver the methods to around 500 teachers before summer 1994. During this period further research and development work will also take place and during the following year a further 500 teacher places will be available on workshops which will incorporate these further developments. Additional funding would allow these already very ambitious targets to be further increased.

Planned development work

Planned development work includes the development of a set of practical investigations based on the *in vitro* production of recombinant molecules followed by electrophoretic separation and identification of the fragments. Technically this will not be difficult. It is also planned to develop totally safe system which incorporates a transformation or a transfection. With an enlightened interpretation of the Genetic Modified

Organism (Contained Use) Regulations (1992) such a system could be granted product release consent allowing its use in the school environment without the necessity for schools themselves registering as GM centres. Only if this is done will we in the UK be able to carry out the more advanced and most stimulating work in the science which is available to school students in the USA and Denmark.

9. *Technical details of the DNA kit*

An electrophoresis tank has been developed from a 100mm 100mm square petri dish. Stainless steel electrodes replace the conventional platinum ones. A stainless steel wire (conger eel fishing trace wire) has been located which will run continually without corrosion. Four lane agarose gels are poured and run on 38 76mm microscope slides. Gels are stained with methylene blue. A second square petri dish is utilised as a stain/destain tank. The electrophoresis runs overnight at 12 volts powered by a domestic AC/DC mains adapter. A transilluminator box with two 6 volt torch bulbs and a square petri dish lid lined with white paper is used to view the stained gel. The transilluminator is powered by the same AC/DC adapter as the gel tank. 1 ml plastic syringes fitted with trimmed pre-marked micropippettor tips substitute for adjustable micropippettors. DNA is extracted from supermarket "cress" following grinding using an SDS buffer which contains only "school friendly" reagents. Although the extraction protocol does make compromises, on electrophoresis around 90 per cent of the total DNA is present as a discrete band of 50kb+. Restriction is carried out with Quadrant trehalose dried restriction enzymes. The extract in TE buffer is merely added to the Quadrant tube which already contains dried activity buffer and restriction enzyme. On restriction the chromosomal band disappears leaving a characteristic nuclear genone smear. Bands from chloroplast DNA can be visible if the restricted sample is concentrated but these are not always clear because of the background of nuclear DNA. This difficulty can be overcome through the initial isolation of chloroplasts so giving a type of DNA fingerprint.

10. *Schools supplied with kits*

Because of difficulty of supply of reagents and assembly of materials funding has been raised to allow the project to make available kits, free of charge, to workshop participants. To date (16.6.93) the following schools have requested and been supplied with DNA kits: Annan Academy, Annan; Warwick School, Warwick; the Leys School, Cambridge; Eton College, Windsor; Queen Elizabeth School, Lincolnshire; Ondle School, Peterborough; Boroughmuir High School, Edinburgh; Drummond Community High School, Edinburgh; Trinity Academy, Edinburgh; St. Mirin's High School, Paisley; Stranraer Academy, Stranraer; Ellon Academy, Aberdeenshire; Duns High School, Berwickshire; Westhill Academy, Aberdeen; St. Stephens High School, Port Glasgow; Johnstone High School, Jonhstone; Greenock Academy, Greenock; Castlehead High School, Paisley; Port Glasgow High School, Port Glasgow; Gryffe High School, Paisley; Mearns Castle High School, Glasgow; Park Mains High School, Erskine; Abranhill High School, Cumbernauld; Earlston High School, Earlston; Christ's Hospital, Horsham; Culford School, Culford; Deben High School, Felixstowe; Maryhill High School, Staffordshire; Vyners School, Middlesex; King Edward VII School, Lytham St. Annes.

Evidence from Monsanto (Dr K M Baker, Europe Director, Public Policy)

PREAMBLE:

While the Sub-Committee has addressed questions primarily to "Monsanto in Belgium", the Belgian entity forms but a very small part of the Monsanto global market and operations. However Monsanto has its European Headquarters located in Brussels and the European share of the global Monsanto R&D activity is approximately 15 per cent, most of which is located in Belgium.

Answers to questions therefore are coloured by the overwhelming smallness of Belgium as a market to Monsanto, but also the high concentration of Management and R&D functions in that country.

1. *How important does your government perceive biotechnology to be?*

In Belgium, the governments, both regional and central have for many years had a substantial focus on the promotion of the application of the new biotechnologies as a source of new economic wealth.

There is a historical reason for this. Much of the early work on genetic engineering had its origins in Belgium, particularly that associated with plants and seeds. It was the team of Schell and van Montagu at the University of Ghent who spearheaded this work, and they were supported by grants from Monsanto in the late 1970's. And several of the modern medical applications of biotechnology arose out of early government generic sponsoring of research at the Universities of Louvain and Liege.

The Prime Minister's Office has had a Science Policy Unit associated directly with the Office for many years. The encouragement of the application of biotechnology and genetic engineering as a source of economic wealth creation has been included in the responsibilities of this Unit since the early 1980's

The Regional Governments have themselves sponsored various initiatives in the past such as "Athena" (Wallonia), "Flanders Technology International" (Flanders), and continue to do so. The Government

Regional Investment Organisations also continue to favour new investments involving the application of the new biotechnologies as an element of both job creation and economic growth, based on the application of new clean technologies.

2. *Which developments in biotechnology are thought to raise safety issues?*

Few developments in the new biotechnologies are thought to raise additional safety issues *above and beyond those normally present in working with biological systems*. This has been demonstrated to be the case in Belgium where for example, a high proportion of the field tests of plants in Europe have taken place with no untoward events, and a high level of local experience has been gained.

For this reason, the Belgian Government in 1992 has introduced procedures for "simplified (regulatory) procedures" to the Community Institutions. It is also the reason that the Belgian Governmemt has attempted to introduce EC regulations in a manner which reflects the general safety risks present in working with genetic biological systems i.e. on a "vertical" basis.

4. *Do regulations distinguish between contained use and general release (for experiment or marketing)?*

Current regulations in Belgium reflect the operation of the N.I.H. (U.S.) guidelines which have been for many years the basis on which experimental systems are operated.

Additional to this, the Ministry of Public Health is attempting to administer biotechnology-related operations on the basis of EC Directives 90/219 and 90/220, *even though these Derectives have not been implemented in Belgium*. This brings with it a distinction between Contained Use and Deliberate Release for administrative and bureaucratic reasons. In practice most focus is on deliberate release-type experiments, although through a "vertical" product sector related Government Department approach.

5. *Is regulation in your country "horizontal" (where a product is judged through the process by which it is derived) or "vertical" (where a product is judged by its characteristics)? Which is preferred by your Government?*

The Belgian Government prefers "vertical" structures for product-based regulations and Ministers have repeatedly said so publicly on many occasions. Operations (that is to say experimental and other work), are considered to be best regulated as part of the normal regulations covering safety and health at work, operation of plant, machinery and laboratories, or environmental protection. Current proposals reflect this philosophy.

Traditionally in Belgium, any experiment involving a biotechnology related operation has been administered through existing "vertical" regulatory systems operated by the appropriate government department responsible for that "vertical" domain. Where necessary, advice is sought from other government departments if there is seen to be a conflict in procedural objectives.

There has been no concept of a "biotechnology industry" requiring separate regulation, precisely because the government has believed that the technology is a tool in the hands of traditional sectors.

6. *What are the consequences of your country's regulatory regime on the competitiveness of your firm, in particular as regards:*

6.1 *research?*

Previously, the general pragmatic approach, and regulation using existing "vertical" regulatory structures in Belgium where most Monsanto European R&D is located, was extremely beneficial to the competitiveness of Monsanto, and therefore Belgium. Application of the new EC Directives 90/219 and 90/220, even in spirit (as the Directives have not yet been implemented in Belgium), is proving to be less of an attraction for research-based activities, in the main because of the uncertainty coupled with the bureaucracy they bring.

6.2 *product development?*

Besides the United States where the majority of Monsanto field tests have taken place, many of our European field tests of plants in the past for the purposes of product development, have taken place in Belgium. Significant benefit has been gained from synergism between the operation a pragmatic regulatory system, a desire on the part of the authorities to encourage installation of employment based on new technologies, and the substantial Monsanto presence in Belgium and its contribution to the local economy.

The Belgian initiative to introduce proposals for "simplified procedures" is based in part on the experience gained from Monsanto experiments in Belgium.

On the other hand, the Community biotechnology-specific regulatory structures for pharmaceutical and veterinary products have had a significant negative impact on Monsanto competitiveness in product development. These regulatory structures which are based on imperfect systems of mutual recognition between the Member States, do not function adequately in practice and lead to internal non-tariff trade barriers being created between Member States of the European Community. This has lead directly to the closure of some biotechnology product development operations in Belgium and also the UK.

6.3 *investment?*

As noted previously, a large proportion of Monsanto European R&D effort is located in Belgium. The operation of a pragmatic regulatory regime is an incentive for Monsanto to consider and compare existing and future regimes in other countries before making investment decisions. This is only one of the considerations, the other main ones being the level of taxation, and wage costs and productivity. Currently, there are no plans to change European locations in the structure of Monsanto's capital investments involving biotechnology.

6.4 *location?*

As the EC structures for biotechnology-based activities begin to be operated, the attractiveness of the United States increases as a place from which to operate.

It should be noted, that excessive uncertainty or impreciseness of regulatory structures, leads directly to reduced productivity and therefore reduced competitiveness. Regions which are burdened with such regulatory structures thus become less attractive as a location for a manufacturing investment, but can still remain an opportunity for product sales. The opportunities for steady employment and job creation are thus diminished, and the region or economic entity becomes merely a consumer and not a producer.

6.5 *sales and marketing?*

Monsanto operates on a global basis and its sales and marketing teams are based accordingly.

In the European theatre, Monsanto has several of its Global Division Headquarters located in Brussels, Belgium. The decisions to locate these Divisions there are not related to the Belgian product regulation structures.

Conversely, European Community product regulatory structures which make it difficult to develop or market products either in Europe, or in any one of the major Member States, would argue for the Global sales and Marketing effort to be located ex-Europe.

7. *Is biotechnology publicly accepted in your country?*

As a country, Belgium has seen few if any problems of acceptance of biotechnology and genetic engineering. There does exist a small number of specialist groups which oppose use of the new technology for various reasons.

The early, very public government promotion of the job and investment creation opportunites offered by new technology including biotechnology may have something to do with this, but this is not sure. Additionally, there is a certain amount of public pride associated with the Belgian scientists who played a role in the early development of genetic engineering.

8. *Has your government implemented EC Commission Directives 90/219/EEC and 90/220/EEC. If so how? If not, when do you expect to do so?*

The Belgian Government has not to date implemented EC Directives 90/219 & 220. The Government expects that this may occur some time this year, although this does not have high Government priority.

The Government in its proposals wishes to implement these Directives in a "vertical" manner, i.e. existing legislation in various operational and product areas will be modified to conform with the provisions of the Directive. It was correctly surmised that implementation of the "horizontal" Directive as approved by the Council of Ministers, would lead to the creation of an excessive bureaucracy, substantial additional costs, and many administrative problems and difficulties with interpretation of the Directives, not the least being an interpretation of what operations were covered and what not. At the same time it was also recognised that safety would not be improved through implementing a "horizontal" system, and could even be diminished.

Implementation of this "horizontal" Directive in the more practical "vertical" manner for administrative reasons has been extremely difficult, and has been one of the reasons for the lengthy delay in implementation.

The above difficulties, coupled with the extreme administrative burden required by these Directives for a small country, have also lead to the Belgian Government officially submitting to the European Commission a Proposal for a "simplified procedure" based on the extensive experience gained on Belgian territory, which would thus modify the Directives as applied in Belgium. The Belgian authorities are thus seeking a more cost-effective regulatory structure which is clearly related to the safety of any particular operation. Experience on Belgian territory is showing that the risks associated with many of the operations associated with the Directives 9EC/90/219 & 220 is particularly low.

Finally, the Belgian authorities are aware of EC Directive 90/679 "Protection of workers from risks related to exposure to biological agents at work" and the need for compatability with Directives EC/90/219 & 220.

Evidence from the Netherlands Embassy

1. The Netherlands' Government considers biotechnology as a key technology for economic development in the future. In the past decade biotechnology research has for this reason been stimulated both at governmental research organisations and in industry. This policy to build up a strong scientific and technological base has been quite successful. An international peer review committee concluded 2 years ago that "the additional funds have been spent extremely well and projected against the international scene, research in biotechnology in the Netherlands has been developed quite strong by, and, taken as a whole, at a good scientific level". In the coming years the focus in policy will be especially directed at societal aspects., regulatory aspects and continuation of innovation policy. The importance attached to biotechnology in the context of international development is reflected in the establishment of a Special Programme Biotechnology and Development Cooperation at the Ministry of Foreign Affairs."

2. It is recognized that techniques of biotechnology (such as genetic modification) are by themselves neutral. Genetically modified organisms (GMO's) are neither inherently risky nor inherently safe. However, due to the relative lack of experience with organisms of which the genetic material has been altered in a way that does not occur naturally, regulation for risk assessement and risk management has been in place in the Netherlands since 1980. Authorisations are required for both the contained use and release into the environment of genetically modified organisms. The existing regulation entails the full implementation of directive 90/220/EC, and to a large extent of directive 90/219/EC. The final details for the implementation of directive 90/219/EC will come into force in the summer of 1993. At this moment, attention is focussing on aspects such as food safety, animal welfare and ethical considerations.

3. No, there is no all encompassing specific regulatory regime for biotechnology in the Netherlands. The Netherlands' parliament has decided to look away for this moment from an integral law on biotechnology. It was decided that there is a need for more experience with the existing regulations and to evaluate those regulations in 1994 in the light of efficacy, transparency and maintainability.

4. The regulation for the protection of man and the environment follows the distinction of the EC-directives 90/219 and 90/220.

5. In the Netherlands, the distinction between "horizontal" and "vertical" legislation does not imply that the one refers to the process by which an organism is derived and the other refers to the characteristics of an organism. "Horizontal" refers to the fact that it crosses several sectors such as different products, whereas "vertical" refers to only one sector or group of products (eg pesticides).

In the Netherlands there are two relevant horizontal (draft) regulations; one existing, the above mentioned regulation for human health and the environment, and one in preparation; ethical aspects of the new biotechnology. The Netherlands further consider anticipating the Novel Foods regulation of the EC by a provisional national measure.

With respect to marketing: after passing the above mentioned safety regulation, GMO's are reviewed like any other product in the same category (eg food, additives, pesticides). The Discussion focussed on the so called one door/one key principle in the marketing phase.

6. There is a lively debate in the Netherlands about the various aspects of the new biotechnology. Especially animal biotechnology is a subject of ethical discussion both in Parliament and in society. The Netherlands' Government sees it as extremely important to have communication between interest groups about sensitive matters such as the new biotechnology. The objective is to create sufficient consensus to have a basis for taking decisions.

7. Yes, by incorporating these in the existing legislation.

Evidence from the Organisation for Ecomomic Co-operation and Development (OECD)—Biotechnology Unit

This note is not a statement of OECD policy.

It has been prepared by OECD staff, with the aim of responding helpfully to the request letter of invitation from the Sub-Committee; drawing upon the work of the OECD expert groups, particularly the Group of National Experts of Safety in Biotechnology ("GNE"), whose mandate (from the Committee for Scientific and Technological Policy: CSTP) is attached as Annex 1.

1. *"The OECD has influenced the development of regulations on biotechnology since the early 1980s. What remains to be done in the regulatory field to:—*

(i) ensure international uniformity; and

(ii) facilitate industry's competitiveness?"

The opening sentence is true, in that the OECD work (both the 1986 "Blue Book" and subsequent publications) are widely cited, rarely criticised, and accepted as authoritative. But they are not prescriptive regarding whether or how national or other authorities should regulate. They provide a common and scientific basis for *risk assessment,* and the OEDC work has developed consensus on principles, concepts and good practices. These have been helpful to regulatory authorities and to legislators. and insofar as they are internationally accepted, address both point (i) and hence indirectly point (ii) above.

However, it is not necessarily feasible or even desirable to "ensure international uniformity" in all respects, given national differences in approaches to *risk management*—a broader subject than risk assessment (see above), and one involving judgements, national styles and traditions, political priorities, etc, and a broad portfolio of potential instruments including statutes, guidelines, codes of practice, standards, education and training, supervision, exhortation, enforcement, etc. In some countries, existing statutes has been seen to provide an adequate basis for regulating the products of biotechnology; in other circumstances, eg the European Community's development of a single market, legislation may be initiated to reduce national differences which would inhibit the aims of that market (although in the case of the EC, still leaving competence as to form and means at national level—cf. Article 185 of the EC Treaty, and Article 3b, on "subsidiarity", of the draft Treaty in European Union).

A general answer to this question is provided by the OECD Council Recommendation of July 1986, which remains relevant in spite of (one could even say, especially because of) continuing rapid advance in biotechnology at the levels of both basic scientific advance, and technological applications. For although some of the questions and uncertainties of 1986 are by now resolved or diminished, others remain, or are raised by new possibilities.

More specifically, question 1 is so close in spirit to the general aims of the GNE, that an appropriate and official response to the question, "what remains to be done?" would be to cite the biotechnology elements of the latest work programme as approved by the CSTP in March 1993; these are therefore attached as Annex 2.

2. *"Do the EC Directives 219 and 220/1990 on 'Contained Use' and 'Deliberate Release' of genetically modified organisms adequately address the safety considerations identified by the OECD for human health and the environment?"*

EC Directive 90/219 on the contained use of genetically modified micro-organisms makes explict use of the "GILSP" (Good Industrial Large Scale Practice) criteria developed by the GNE and published in 1986.

The question of adequacy is difficult to answer, in that EC Directives are addressed to Member State governments with a view to the introduction of national legislative measures so far as necessary to give effect to the aims of the Directives. The adequacy with which safety considerations are addressed in a given national environment will therefore depend upon several other factors including other national and Community legislation, questions of interpretation and application, efficiency and thoroughness of oversight and enforcement.

Assessment of adequacy is further complicated by the dynamic character of the progress of scientific knowledge and cumulative experience. In response to this, the EC Directives themselves include provision for adaptation (except to their scope); "adequacy" is therefore the outcome of an envolving balance (ideally, a "match") between the focus and stringency of oversight, and the state of scientific knowledge of risk assessment. In effect, if no safety considerations are found, *any* means would be "adequate" or "more than adequate". (Of course there *are* safety considerations, eg, in handling dangerous biological agents; but these are not specific to biotechnology, and may be "adequately" addressed by other means—such as EC Directive 90/679 on worker safety vis-a-vis risks of exposure to biological agents).

For the above reasons, the OECD could not provide a simple answer to the question, other than the above general points; and has neither the resources nor the intention to monitor in detail the various national situations. It does, however, seek to assist national authorities by the collection and diffusion of the collective experience—for example, via the "BIOTRACK" database on field releases.

3. *"Future development in regulation could accelerate the trend away from "horizontal" process-based regulations towards "vertical", product-specific regulations. What are OECD's views on this trend with regard to the economic and social impacts in members countries?"*

The OECD expert groups have not explicitly considered the trend referred to. It is nonetheless true that in recent years, the basic work of the GNE has been pursued through a growing number of groups specialising in specific product categories—terrestrial food products, aquatic food products, crop plants, bio-fertilizers, vaccines, bio-remediation agents, and others envisaged. But no assessment of impacts of such a trend have been conducted.

Expert study reports have been published by OECD, including

(i) "Biotechnology, Agriculture and Food" (1992);

(ii) "Biotechnology: Economic and Wider Impacts" (1989);

(iii) "Biotechnology and the Changing Role of Government" (1988).

Of these, the first two are indeed in some degree assessments of socio-economic impacts; but of biotechnology in general, not of the trend referred to. The third report comes closer to the latter point, in focussing upon problems of in inter-agency or inter-departmental policy co-ordination, in relation to a pervasive technology which raises issues in the fields of interest of an ever-growing number of Ministries. OECD has within its own activities in biotechnology, and in recent requests to governments concerning views on the future of these activities, urged effective co-ordination to cope with this multi-dimensionality; but the trend itself seems inherent in the pervasive character of the technology, and therefore not a matter on which opinions could usefuly change the reality.

4. *"What will be the impact of biotechnology on employment in agriculture and food production in member contries?"*

In the report (i) referred to under Question 3, the 15 expert authors participated in preparing a summary of the policy-relevant conclusions of their work, The result is attached as Annex 3; and within this list of seven points, number 5 may be relevant to this question.

For a more detailed justification of this judgement, reference should be made to the report—in particular to section 6, "Impacts on Employment" of Chapter VIII, "Economic Impacts"; attached as Annex 4 to this note.

5. *"When and how will the under-developed world benefit from biotechnology?"*

Again, reference might be made to point 7 in Annex 3, the policy conclusions of the report on "Biotechnology, Agriculture and Food". Reference could also be made to various study reports prepared by the OECD Development Centre, concerning the diffusion of agricultural biotechnology in various sectors.

It is clear that biotechnology will have significant and varied impacts on developing countries, including many positive factors such as:

(i) improvements in health status of populations, especially via cheap and effective vaccines—cf, the hepatitis—B vaccine (produced in a recombinant yeast host organism);

(ii) improvements in agricultural productivity (virus-free cassava, bovine growth hormone, animal vaccines—eg for rinderpest, better and faster diagnostics for plant or animal diseases);

(iii) access to world markets, with corresponding benefit to low cost primary producers, facilitated by tests and protection measures enabling the producer to satisfy the sanitary and phyto-sanitary requirements of developed country markets;

but also disruptive changes such as lower price for commodities on which some producer countries are heavily dependent, due to substitution effects.

For a fuller consideration of developing country impacts, reference could be made to recent papers by Dr. Albert Sasson of UNESCO; who with a wealth of examples, emphasizes that no developing country is excluded from biotechnology. Its essential role is emphasized by practically every other UN agency—especially WHO, FAO, UNIDO and UNEP; see also Chapter 16 of AGENDA 21, as adopted at the 1992 UNCED ("Earth Summit").

On a more general point, it is clear that the cultivated and grazed areas of the planet cannot be significantly further increased, or should even be diminished (for conservation reasons) while world population may achieve a further doubling before possibly stabilizing; and that some current agricultural practices (in both developed and developing countries) are unsustainable, degrading not only the environment, but the long-term agricultural productivity of the lands concerned. Given these strategic facts, the relationship of further progress in bioscience and biotechnology to developing countries is not so much one of aggressive impact and doubtful benefits; but of indispensibility. This is clearly recognised by policy leaders in all major developing countries, as indicated by their published statements on biotechnology, and by their research expenditure and actions.

"Thus the short answer to the "when" part of the question must be, "already now; and increasingly over coming years".

Annexes

1. Mandate of the GNE, as adopted by CSTP, 1988.

2. Biotechnology elements of the 1994 Work Programme, as adopted by CSTP, March 1993.

3. Summary of policy conclusions from the report, "Biotechnology, Agriculture and Food" (OECD, 1992).

4. Section VIII.6, "Impacts on Employment" from the report, "Biotechnology, Agriculture and Food" (OECD, 1992).

ANNEX 1

Mandate of the OECD Group of National Experts on Safety in Biotechnology

(as established by the Committee for Scientific and Technological Policy, 1988, on the occasion of renewing the earlier, 1983, mandate. The mandate is being further discussed with a view to renewal and possible modification during 1993.)

Group of National Experts on Safety in Biotechnology

The Group shall, under the guidance of the Committee for Scientific and Technological Policy, follow and keep under review safety issues in biotechnology with a view to developing a common scientific basis for its safe use and to fostering international harmonisation of safety practices and procedures.

In this work the Group shall, considering ecological as well as human, animal and plant health issues, and with particular reference to the large-scale industrial use of genetically modified organisms and to their introduction into the environment for agricultural and/or environmental purposes:

(1) keep under review and develop scientific principals relevant to the evaluation of organisms including criteria for classification/categorisation of these organisms for the required purpose;

(2) on the basis of these principals, develop appropriate good safety practices and/or guidelines, and update existing ones;

(3) consider ways and means to promote the harmonisation of definitions, guidelines, principals, or codes of practices in areas pertinent to the use of the above-mentioned organisms;

(4) further promote the international exchange of information on and experience with risk assessment including methods and other related aspects comprising data base networks;

(5) follow the development of national guidelines and regulations;

(6) promote approaches on public information about the application of biotechnology.

The work of the Group will be co-ordinated with that of the Environment Directorate. The Group shall report to the Committee for Scientific and Technological Policy, while keeping other Committees—in particular the Environment Committee and the Committee for Agriculture—informed on the progress of work.

ANNEX 2

Biotechnology elements (partial extract) from the (currently discussed) 1994 Work Programme of the Committee for Scientific and Technological Policy.

Theme III: Biotechnology.

Activity 7: Biotechnology—Safety-related and Other Public Policy Issues, including Scientific Follow-up on Biotechnology for a Clean Environment.

I. *Objectives*

(A) To continue developing and/or refining and updating principles, practices and criteria for the safe use of living modified organisms and their products in industry, agriculture, health care and environment, and to encourage and facilitate their international harmonization.

(B) To follow up work on biotechnology for a clean environment, and particularly to organise two scientific workshops on specific, topical issues related to the contributions of biotechnology to environmental quality, with the aim of:

- formulating policy recommendations to OECD Member countries.
- exploring the potential and the mechanisms for increased international R&D co-operation in environmental biotechnologies.

(C) Subject to the adoption and the specific content of a renewed and revised mandate, the preparation or initiation of a review of priority issues arising from the biological sciences and biotechnologies, identifying topics where the OECD could make an essential and cost-effective contribution.

II. *Background/rationale and Proposed Programme*

The Group of National Experts on Safety in Biotechnology was created by CSTP in 1983. The first resulting report, "Recombinant DNA Safety Considerations" was published in 1986. Part of the follow-up programme aimed at developing further, refining and updating the general safety guidelines in the light of scientific developments and accumulated experience was completed in 1991 with the achievement of generic principles for small scale environmental releases (Good Developmental Principles, "GDP") and the updating of GILSP

(Good Industrial Large Scale Practice) safety criteria for recombinant organisms used in industrial production. Reports on GDP and GILSP were published together as "Safety Considerations for Biotechnology 1992". Work has continued also in the following areas: (i) large scale releases into the environment, including the completion of a general statement of safety principles (the "Preamble" document); specific work on crop plants, including a Historical Review of Traditional Crop Breeding Practices; and the development of a programme of work on various categories of micro-organisms, including biofertilizers, live vaccines, and others; (ii) safety assessment of food produced by biotechnology, from terrestrial and aquatic organisms; (iii) analysis of field release experiments. Reports in several of these areas are nearing completion or are complete and awaiting derestriction or publication.

Proposed Programme:

Safety-related work in 1994 will focus upon:

- completing guiding principles for safe large-scale use of the varius categories of modified organisms referred to in (i) above—ie, crop plants (may be completed in 1993); completing or continuing corresponding work for the above-mentioned and further categories of micro-organisms (eg, biopesticides, bio-leaching/bio-mining agents, bio-remediation agents, biofeeds) and for transgenic animals, including insects and fish;
- completing guiding principles for food safety of modified aquatic organisms;
- pursuing the parallel review of monitoring methods for the modified organisms mentioned above (in collaboration with the Environment Directorate).

Clean Environment work: during its third meeting on 11–12 January 1993, the Ad Hoc Group of Government Experts on Biotechnology for a Clean Environment agreed to ask the Committee to include into its 1994 programme of work, subsequent to the completion of the report "Biotechnology for a Clean Environment" planned for 1993, a follow-up activity comprising the organisation of two scientific workshops. The Ad Hoc Group agreed to submit to the Committee three, provisional, workshop themes for further reflection and selection; workshop reports to be submitted by end of 1994. These themes can be made more specific or narrow, if necessary.

Theme 1: Biotechnology for Improving the Management of Material Cycles

This covers the issues of renewable resources. To make it more specific, it could be limited for example, to more efficient water use and recycling.

Theme 2: Long-term Applications of Biotechnology for Global Environmental Quality

This includes global problems which could be addressed by national/local biotechnology solutions, such as the biological potential for carbon-absorption at ocean surface waters.

Theme 3: Efficacy Measures for Standardized Performance Evaluation and Predictability in Bioremediation

Experts consider this as one of the most important issues for the future of bioremediation.

Following the discussion of the programme of work by the Committee, the Ad Hoc Group intends to discuss the follow-up proposals again during its fourth meeting on 1–2 July 1993.

This activity will be closely co-ordinated with the Group of National Experts on Safety in Biotechnology (GNE) which started work on bioremediation safety in 1993, and with the Environment Directorate which intends to make a contribution to "Biotechnology for a Clean Environment" in 1994, focusing, however, on regulatory and diffusion aspects, rather than R&D. The present proposal has already been discussed with the Environment Directorate which will be closely associated with the activity.

Other work is dependent upon the outcome of 1993 discussion of the future mandate, but is likely to require an initial review and preparatory phase during 1994, as basis for discussion with Member countries of the priorities for OECD action.

III. *Methodology/output*

Work on all the above issues will be carried out through lead-country contributions and/or outside consultants-experts in close association with the Secretariat. Reports will be prepared for the CSTP as materials are compiled and presented to the Group of National Experts and/or the Ad Hoc Group.

Consultations with Member countries on particular scientific and technological issues as well as countries' additional finnancial support will be necessary.

The programme will be co-ordinated with the relevant activities on biotechnology of the Environment and other interested Directorates.

ANNEX 3

from: "Biotechnology, Agriculture and Food" (OECD, 1992)

Policy Conclusions (Formulated by the experts and a working group chaired by Sir Barry Cross).

1. Biotechnology can be applied to all plants, animals and micro-organisms for food and non-food uses, thus affording the opportunity profoundly to improve the quality and efficiency of agricultural production.

2. New agricultural and food biotechnolgies are extensions of traditional genetic modification practised in animal and plant breeding throughout civilisation, but further progress depends upon support of the basic sciences from which they have sprung.

3. During the next few decades, agriculture and food biotechnologies can make a vital contribution to global economic and social welfare for a rapidly expanding human population.

4. Biotechnology has the capacity to limit the damaging environmental consequences of some agricultural practices, deforestation and climatic change.

5. Contrary to earlier negative predictions, the diffusion of agricultural and food biotechnoligies in the OECD area in the next ten years will be a gradual process without major, destablishing impacts on social structure or employment.

6. Public perceptions of biotechnology and safety issues remain potent sources of industrial uncertainty and must be addressed by improved communication among governments, scientists, industry, the media and the public.

7. Agrofood biotechnology could make a crucial contribution to the health and prosperity of the Third World, and it is therefore in the economic interest of both OECD and developing countries to devise, in concert, policies on research, intellectual property, safety, etc, that will enable the latter to build up their biotechnology capability.

ANNEX 4

from: "Biotechnology, Agriculture and Food" (OECD, 1992)

6. *Impacts on Employment*

Biotechnologies could exert an influence on agricultural employment by two routes: a direct one by application in agriculture and an indirect one by application in upstream and downstream sectors. In both cases the impacts could be job-destroying or job-creating. Furthermore, results will be different for closed or for open economies and particularly for well protected or less protected agricultural sectors. The impacts on structure, in international trade and competitiveness and on employment are obviously closely linked (OECD, 1989).

Total employment in agriculture shows the employment potential which might be affected. As has been pointed out, the share of agriculture in total employment is declining in OECD countries. The OECD total fell from 10.6 per cent in 1978 to 8.9 per cent in 1985. In highly industrialised OECD countries with large farms such as the USA and the United Kingdom, the share declined to 3.1 and 2.5 per cent in 1985, respectively. Mediterranean countries reach proportions of 23.1 and 23.9 per cent for Portugal and Greece respectively and 57.1 per cent for Turkey. As the economic, political and technical forces behind this secular process are still at work, further declines in agricultural employment can be expected. However, for the first group of countries, the potential for further decline is now quite limited, whereas the latter group has a substantial potential for further employment reductions and has in fact, experienced high rates of decline in the recent past. Biotechnology, as one major source of technical change among others, will contribute to this trend.

However, even in highly industrialised countries with low rates of agricultural employment, concern about expected negative employment effects of agricultural biotechnologies has stimulated the rise of countervailing powers to limit their application. Much opposition against the sugar substitute isoglucose, in Europe, and against bST, in various countries, has been the result of such employment concerns.

However, the central questions for the future go widely beyond biotechnology. Will agricultural protectionism be reduced, and if so, at what pace and to what extent? If agricultural protection falls, employment in agriculture will decline, but employment in other sectors will increase due to the "welfare effects" of larger resources being made available elsewhere. Depending on the policy path chosen, the overall effects could be much larger than the impact of biotechnologies alone. For the adjustment of the farming sector, however, the combined effect of all influences is relevant. Policies therefore should take into account effects from both biotechnology and from a reduction of agricultural protectionism.

It has been argued that biotechnology might help to develop new non-food products based on agriculture and thus create new jobs in agriculture. However, assessments in Germany indicate that the potential short-term effects will be small (Meinhold, 1987), principally because of the still insufficient profitability of renewable resources in general.

Depending on the price policy pursued, rates of annual labour reduction in agriculture of between 1.5 per cent, for an income-oriented price policy, and 5.5 per cent, for a market-oriented price policy, have been projected for the period 1986 to 2000. In Germany, agricultural labour units would decline from 560,000 to 460,000 in the first scenario and to 234,000 in the second scenario. Production of new renewable resources is projected to employ not more than approximately 13,000 labour units in agriculture, and only with government support. Unless this production uses idle land, it will merely replace food products and hence, at best, reduce the rate of decline in the agricultural labour force. It must be stressed that these are short-term estimates. In the longer term, a growing conversion of agriculture to non-food products could lead to additional employment opportunities, but this cannot relieve current pressures on agriculture.

Use of biotechnologies in upstream and downstream sectors will directly influence employment in these sectors and indirectly impinge on employment in agriculture. New jobs in the downstream sectors might be created by quality improvements in food and by non-food uses of agricultural products. In large-scale, capital-intensive processing units the employment effects will be minor. However, if biotechnologies could be used for the development of new high-value food niches and decentralised renewable resources production ("agro-refineries"), the employment effects are likely to be more substantial. Direct employment effects in upstream sectors are closely linked to the demand for agricultural food and non-food products; in addition, employment shifts can be expected between agrochemical and biotechnology sectors and within companies. The indirect employment effects in agriculture due to biotechnology induced changes in upstream and downstream sectors cannot be evaluated at this time.

Countries with open economies, less protected agricultural sectors, and a large potential for development of agricultural biotechnologies, will win international market shares and hence protect agricultural employment by scientific and market forces, but this will come partially at the expense of slow adopters and with no guarantee of a globally positive net effect, However, as in the case of renewable resources, this effect will in general merely reduce the rate of long-term decline of agricultural employment.

Letter to the Chairman from Pharmaceutical Proteins Limited (Ron James, Managing Director)

May I thank you and your Committee for giving me an invitation to submit further written evidence. I had not personally submitted written evidence earlier because I only learned of the enquiry indirectly and at a late stage. I hope that my experience was not widespread among smaller biotechnology based companies because the views of this sector are, in my view, disproportionately important. The reason I hold this belief is that in the USA, smaller recently formed companies are the engine of a biotechnology industry which is a significantly larger part of the USA economy than is currently the case in the UK,and the views of smaller companies may be important in understanding the reasons for the difference.

Having been given, through the BIA, the opportunity to state the case for changing the thinking behind regulation of the industry, I wish now to concentrate on 3 other issues,—the importance of biotechnology to the UK; finance for high technology based early stage companies and patent protection for biotechnology inventions. However, before doing this, may I briefly present my credentials for doing so.

Credentials

I obtained a degree in chemistry through part-time study while employed as a technician in the research laboratories of Glaxo. I then acquired a PhD in organic chemistry and went on to spend several years in industrial research and research management before moving to technology transfer and patents administration. During this period I obtained the Certified Diploma in Accounting and Finance, and later joined the Prudential's Ventures Capital team with a responsibility for health-care and biotech investments. Having been a founder investor (1987) (with the Prudential's money) and non-executive director of Pharmaceutical Proteins Ltd (PPL), I joined that company in 1989 as its Managing Director.

PPL occupies a world leading position in the production of human therapeutic proteins in the milk of transgenic animals (sheep). The Company now employs 50 people, has collaborations with multinational pharmaceutical companies in Europe, USA and Japan, and with biotech companies in USA. Last year revenues exceeded £1.5 million, all but £30,000 coming from outside the UK. The Company has been funded by venture capital (four rounds) provided by investors based in UK, USA, France and Japan (in fact 40 per cent of the Company is now owned by non UK investors). We expect to obtain a public listing for the shares in the Company, either in UK or USA, early in 1994. PPL recently acquired a small Virginia (USA) based company which operates in the same line of business.

The Company's technology enables it to produce thereapeutic proteins at substantially lower cost than any alternative method of production, thus benefiting shareholders, employees, patients and the UK economy.

Why is Biotechnology important to the UK

Having read the written submissions of the BIA, SAGB and CBI, all stress the size of the industry which, to a greater or lesser extent, depends on, or benefits from, biotechnology.

While not disagreeing with these projections, I would like to approach the question from a different standpoint.

It is first necessary for us to agree that the UK cannot survive with an economy which is predominantly service industries, since imports cannot be paid for by service industry which has little opportunity to earn foreign revenues. By definition (the city and tourism apart) services are rendered by one UK entity to another.

The UK is increasingly finding it difficult to compete in the older labour intensive manufacturing industries. If we are to maintain our standard of living and pay for the necessary imports we must move towards a high wage/high added value situation which means investing in and nurturing new high technology industries which maximise the benefits to be gained from exploiting the UK's excellent science base.

Biotechnology is but one example of high technology, but it is particularly important because of the range of product sectors that will make use of it. It is for this reason that both the US government and that of Japan has recognised and publicly stated that biotechnology is important. Currently the UK ranks second behind USA in the exploitation of biotechnology, but it will not be long before we are overtaken by Japan, which came much later to this sector.

So put simply biotechnology is important to the UK because we need to manufacture and to export. We find that increasingly difficult in "sun set" industries so we must concentrate on high tech industries of which biotech has a major impact. The UK government should recognise this importance and do all it can to help the industry. Only a positive stance (ie not just neutral) can keep the UK in the top league, and underpin our future standard of living.

Funding for the Industry

Nobody would argue with the view that some of the UK pharmaceutical companies are world class, and are now, somewhat belatedly in some cases, making effective use of biotechnology. Because of the excellent profit performance of these companies, there is no funding difficulty there. The funding problem lies with the small entrepreneurial companies, both those which already exist and the many more which probably should exist. Dr Nesbitt identified the difficulty of obtaining what he called the "pre-public" phase financing, which hopefully will be lessened with the proposed easing of the requirements for a stock market listing which the London Exchange is considering, but that alone may not be enough without a change in investor attitudes, which are in turn partly related to the overall perceptions of biotechnology.

At least as serious is the relatively small number of biotech companies which manage to get started. Much of the UK so called venture capital industry does not invest in wealth creating ventures, but recycles ownership of existing business through funding management buy-outs and buy-ins, or provides developmental capital for low tech (often retail or service based) industries. While there is nothing inherently wrong in this, it is not doing anything to creat the high added value products which will be exported to pay for imports, and which will be important in sustaining the UK's standard of living. Tax breaks for gains made by investments where a given percentage has been invested in longer term higher risk, high tech, perhaps initially non-profitable industry should be considered.

In addition, some pump priming investment by government on behalf of the tax payer can be justified. The DTI is doing some through LINK and SPUR etc. but these grants are directed towards supporting academic involvement or marginal projects which would not be funded without grant aid. It must be commercially sensible to aid instead, cover projects which were of mainstream importance to the companies. Under such circunmstances, the companies would probably spend more overall on the project (and thus do a better job), and the "subsidy" would help attract venture funding. Capital grants, set off against future corporation tax would benefit non profitable companies in the way that established profitable businesses have recently been helped by tax allowances for captial items. Such temporary concessions are of no value to growing companies not yet making profits, so not yet able to take any adavantage of reduced tax bills, and it is just such companies where the help is most needed and would have the highest ultimate beneficial effect.

I would also draw the select committee's attention to the grant given to small businesses for investigating new products by the National Institute of Health in USA. The DHSS has no such mechanism to support the development of new health-care products.

Finally, I cannot leave the subject of finance without commenting on Lord Renwick's comments on Dr Nesbitt's evidence. Lord Renwick stated correctly that "shareholders do like dividends" and indicated that he thought 10 years was a long time to wait for a return, Investments of the sort we wish to encourage will provide a significant capital gain as the value of the equity purchased increases, and this should offset the need for short-term dividends. However, an earlier means of trading such shares would reduce the time such shares need to be held. The widespread short-term desire for dividends may mean that there is eventually no long-term growth industries in the UK to invest in. While this may be of little consequence to the investor who could then invest overseas, it would be detrimental to the UK economy.

Lord Rewnwick also noted the often quoted assertion from the city that there is no shortage of money for good projects. The problem here is that the city's view of a "good project" is one that gives high returns in a short-term with minimal risk. This short termism is one that gives high returns in a short-term with minimal risk. This short termism is not seen in USA, much of the rest of Europe or in Japan. Lack of investment has already cost the UK ownership of, and manufacturing jobs in, cars, motorbikes, TV's etc etc. It is also resulting in UK biotechnology based companies having to obtain funding from outside of UK with the consequence that ownership and ultimately the gains will also go overseas. Unlike the large companies represented by SAGB, the small biotech company cannot in general choose to do its business overseas. It depends on the talents of groups of people who are not collectively mobile. If funding is not obtained, or the regulatory environment is not supportive these companies cease to exist.

Patent Issues

It is essential for the continued funding and development of biotechnology based industries that inventions involving "living matter" should be able to be protected in exactly the same way that inventions in other fields are protected.

The *only* reason that companies wish to protect biotechnology inventions is to be able to prevent their competitors gaining from the results of investments, often over a long period, in research to produce new products and processes, without having to a have made similar investment in R & D. If, having done all the work to develop a new product or process, a competitor could copy it for free, no-one would undertake such R & D in the first place. I know from experience both sides of the venture capital business, that one of the first things a potential investor checks is a company's patent position.

I should also stress at this point that the industry is not seeking a special position. Biotechnology inventions should satisfy exactly the same criteria of novelty, non obviousness and utility that apply for all patentable inventions, and moreover it must meet the requirement of a description of how to work the invention that could be followed to obtain "without undue experimentation" the desired result.

It follows logically from this, in my view, that certain things are not, or are not now, patentable. For example, new varieties obtained by *conventional breeding* which did not require the intervention of man are not patentable because the results are not reproducible. This is most obviously seen in plants obtained by cross pollination (as opposed to self propagation) where every seedling will be different. Thus it is impossible to describe how to produce a particular seedling. This logically leads to plant breeders rights for new plant varieties rather than patent protection. I also believe that there is no longer any invention in isolation and cloning, say, a human gene (or less so a mere part of a human gene). Such isolation, cloning and sequencing are now all known techniques and the gene itself is not new (novel) because it occurs in nature. There are however many true inventions, including in some cases combinations of parts of genes which do not occur together in nature and which have some practical non obvious benefit. Such true inventions deserve protection.

The patentability of biotechnology inventions is under threat from two directions. There are arguments proposed by various lobby groups opposed to biotechnology, who are using an attack on biotech patents as a way to inhibit the development of biotechnology, and the related requirement which the European Commisson wishes to impose only on biotechnology patents of taking into account socio-economic and moral factors in deciding patentability.

These threats apply to all patents relating to living matter, but are especially acute in the case of transgenic animals and plants. Indeed, in a recent emergency debate, attended by an unrepresentatively small number of MEP's the European Parliament accepted a motion which called for the European Patent office to uphold the appeal against a patent for Dupont's "oncomouse" and also called for a ban on the granting of any other animal patents pending on clarification of the issues. The matter must therefore be taken seriously.

I will deal with the reasons put forth by the anti patent group for not granting patents in this area.

One of the arguments put forward is that the monopoly provided by a patent on a genetically modified plant or animal would be used to increase prices and would put small farmers out of business. This is economic nonsense and ignores the fact that farmers are free to continue to use the "old" modified product. Only where the economic gain to the farmer of using the patented product is greater than the additional cost, will the farmers buy the new product. That situation exists today with new varieties protected by plant breeders rights, and patented plants or animals would not change this. It also ignores the fact that seed companies will continue to compete with each other, and that if prices exceed costs by too large a margin, this will attract new companies into the business, maybe selling "old" varieties at lower prices. This is what the free market economy is all about.

A second issue is the proposed ownership by third world countries, of genes which are found in plants or animal found in these countries. This is a complex question, but the illogicality of the concept may be illustrated by the following questions—

Do I own the vanilla in the seed pod of an orchid that grows in my greenhouse and do I own the gene which controls the production of vanilla?

If a tree grows in Nigeria, Bolivia, Japan and China, who owns its gene? Or if an animal strays across a national border?

If a plant exists only in Brazil and the Brazilians are about to make it extinct by clearing the forest where it is found, can the rest of the word complain about the lost genes?

The International Undertaking on Plant Genetic Resources of the UN Food and Agricultural Organisation take the view that genetic resources are the common heritage of mankind, and there is logic in this view. What is beyond question is that ownership of genes is a completely separate issue from ownership of patentable inventions based on such genes. In similar vein, animal welfare groups argue that a patent on an animal invention is wrong because man does not own animals, yet farmers believe they own the animals they buy and sell, and many believe they own their pets.

The real "mad hatters tea party" begins when moral and socio-economic issues are applied to patentability.

It is important to remember here that a patent gives its owner no rights to do anything except to prevent another working his invention. It does not confer a right on the owner to work the invention and therefore other laws concerning what is right and wrong continue to apply. It follows that if society wishes to prevent some practice, it should legislate against that practice not stop patents related to the practice. A ban on patents is a crude implement which hits good and bad indiscriminately.

More perverse is the fact that a ban on animal patents will have exactly the opposite effect to that desired by the animal rights supporters. Let me give two examples.

If "oncomouse" were not patented, now that it is known how to produce such an animal, anyone would be free to make oncomice and to use them or sell them. Without the monopoly, prices maybe less and more oncomice would be used not less. Moreover if only Dupont can produce and sell oncomouse it is possible to monitor their production and use whereas if all can produce them, such control is virtually impossible.

More perverse is the case of so called "Upjohn mouse". These transgenic strains of mice have been produced to test hair growth formulations and when the formulation works, it triggers the expression of the product of an introduced marker gene, the action of which can be observed. The patent applied for gave several examples of marker genes which could be used and claimed these as inventions. The patent office considered the moral question and decided that the expression of the marker gene caused no suffering except where the marker was an oncogene which caused the animal to develop tumours, and that for such an application the degree of suffering was unethical. Thus claims were allowed for all cases except the oncogene marker. The result of this is that no-one except Upjohn can use mice with the acceptable marker genes, but everyone else is now free to use mice with the one gene which will cause unwarranted suffering!

Patent examiners are not the right people to judge what is moral or whether the socio-economic impact of an invention is disadvantageous. Such decisions should be taken outside the patent system. The current appeal to the granting of the oncomouse patent instigated by the BUVA and other animal rights group is based only on whether the examiner properly took into consideration all the moral issues. Each and every biotech patent granted is likely to be challenged by the lobby groups on such moral grounds and much time and effort will be spent arguing these issues which have no place in the patent system. Once again biotechnology has been singled out for special treatment. It may soon be impossible to get a patent for oncomouse, while patents on the fabled better mousetrap will be granted!

The final point to consider concerns freedom of information. By and large, the public wants to know more about what biotechnology companies are up to. The trade off for a monopoly for a limited period is public disclosure of the invention. Without patents, biotechnology companies will attempt to protect their developments by keeping what they do secret. Patents allow more openness.

I urge your Lordship's committee to use their influence to bring about a situation where patents on living matter are treated in the same way as all other patents, and to separately legislate to limit or prevent those specific developments felt to be wrong on a case by case basis. Patents are an inappropriate battlefield on which to sort out these issues.

Thank you for allowing me to present my views.

Evidence from Ross Breeders Limited

EXECUTIVE SUMMARY:

Ross Breeders Limited are primary breeders of broiler (meat) chickens. A wholly owned subsidiary of Hillsdown Holdings Plc, Ross Breeders is one of the three largest poultry breeders in the world, with over 70 per cent of turnover being generated overseas. In 1992, Ross Breeders won the Queen's Award for Export Achievement for the second time in five years. Ross Breeders exports to 60 countries around the world and has an operation in the USA which supplied 30 per cent of the US Market, as well as Central and South America. Joint Ventures agreements exist with grandparent operations in Hungary, Turkey, Spain, New Zealand, Zimbabwe and the Czech Federal Republic and programmes to supply pedigree stock exist in Brazil, India and South Africa.

Modern poultry breeding is a technology intensive industry and Ross Breeders lead in a number of applications. These include automated data acquisition and handling, monitoring of bird performance, diagnostics and genetic analysis. Our industry is served by the application of biotechnology at many levels, eg enzymes produced as feed additives, novel vaccines, competitive exclusion for improved poultry and human health and spin-offs from general recombinant DNA technology which give us better genetic and disease diagnostics and the potential for genetic manipulation.

RESPONSES TO SPECIFIC QUESTIONS:—

1. *What is your interest in biotechnology?*

We stand to benefit in two ways:

(a) Indirect or spin-off products of biotechnology which enhance our breeding programme efficiency.

(b) Direct application of biotechnology to produce genetically manipulated chicken lines is now practical.

2. *How and why is biotechnology important to the UK industry?*

To remain competitive we must ensure the incorporation of relevant spin-off technologies to our breeding programmes and the direct application of recombinant DNA technology where effective. Our present health status, diagnostic efficiency and breeding programme success has been based on timely application of these technologies.

3. *What future prospects and opportunities does the technology offer?*

Maintaining and improving the UK (now European) health status is an important factor in retaining competitive breeding companies. The application of biotechnology to novel vaccine manufacture and related spin-off technologies will remain vital.

The genetic manipulation of chickens for various characteristics may become an important aspect of product competitiveness.

All the technologies are now available and practical, judging the appropriate genes for manipulation and the timing of the product development are now the important issues.

4. *Which developments in biotechnology raise issues of safety and how should they be addressed?*

All developments raise issues of safety and they must be referred to expert groups. With experience, the risks associated with some procedures may be recognised as so limited that a lower level of regulation is acceptable. Risk assessment must guide the nature and pace of developments given that the moral case for such developments is accepted. Need should be judged by product acceptability and should not be confounded with safety, efficacy or quality considerations.

5. *Should biotechnology be regulated by an industry specific regime?*

Yes. The expertise is available, and examples for the framework already exist, eg for the pharmaceutical industry.

6. *Is horizontal regulation better than vertical regulation?*

No. Vertical regulation suits industry needs better.

7. *Should regulation evolve from a horizontal to a vertical approach in each industrial or environmental application?*

A scheme that reflects product development paths would simplify the regulation process eg genetically manipulated chickens producing food products should have a single integrated regulatory procedure. Genetically manipulated chickens producing pharmaceutical products in eggs should have a separate procedure.

8. *How do current regulations compare with those of other competitor countries?*

(a) EUROPE

We are concerned that harmonisation will imose the most inhibitory system on all the EC countries. In the meantime regulation in non-EC countries continues to diverge. Our only European competition originates in other EC countries with similar systems to the UK.

(b) FAR EAST

We have no major competitors here currently but the early acceptance of foods from genetically manipulated species may lead to alternative breeding programmes being established in the Far East using biotechnology.

(c) USA

Our major competitors are currently based in the USA. Conditions for the development of the biotechnology have been more favourable in the USA than the UK. This has led to technical centres of excellence which will in turn stimulate industrial collaboration. We are not excluded from establishing our biotechnology programmes in the USA in our US subsidiary. More permissive regulatory systems especially at the level of "need" in the food industry, suggests that the USA wants to be the centre for this technology.

(d) SOUTH AMERICA

A number of countries in South America (particularly Brazil) have substantial poultry industries and a good science base. As in (b) above, new competition may emerge from these countries with early acceptance of the technologies and relatively permissive regulation.

9. *What are the consequences, or likely consequences, of the regulatory regime on competitiveness of the UK industry, in particular as regards:*

(1) *Research*

The research here in the UK is weak in the "near market" areas. We would seek collaboration in centres of excellence and these have flourished in the USA and Canada. Although largely UK based at present our in-house research spending would follow regimes which gave the best balance or scientific advantage, regulatory support and product development potential.

(2) *Product development*

The EC represents only 14 per cent of the world's chicken meat production and 13 per cent of its consumption. Present attitudes in the EC suggest that transgenic meat products would be treated as "novel foods" and be subject to a fourth criterion of "needs" for approval. The larger markets may have different criteria and approve such foods leading to the world market splitting into sectors based on biotechnology acceptance or rejection.

(3) *Investment*

This would anticipate and follows market development. On present evidence, investment would only reduce in the EC as a proportion of the total.

(4) *Location*

I refer to my answers to question 8 and 9(1), 9(2) and 9(3).

(5) *Sales and Marketing*

I refer to my answers to questions 9(2) and 9(3).

10. *Is there danger that the present regulatory regime will prevent exploitation by British industry of research conducted in the UK science base?*

Yes, it is already happening.

11. *How best can issues of public acceptance be addressed?*

An effective and consistent regulatory regime could contribute significantly to public acceptance. The balance between listening to public concern and facilitating responsible industrial development will always be difficult but the regulatory authority can establish confidence in the public. It would also encourage UK-based development because approval by a reputable regulatory authority would lend a product credibility in other markets.

12. *What other factors do you consider will play a crucial role in the competitiveness of the UK biotechnology industry?*

Good training and a career structure in "near market" government sponsored research which ensures efficient technology transfer.

Evidence from Margaret Sharp and Simon Shackley

Evidence from Margaret Sharp and Simon Shackley, respectively Senior Fellow at the Science Policy Research Unit (SPRU) University of Sussex and Research Associate at the Centre for the Study of Environmental Change (CSEC) at Lancaster University.

1. *Interests in biotechnology*

Margaret Sharp has been working in fields related to biotechnology since the early 1980s. Her main interests have focused on developments in the UK and Western Europe and in particular the way in which Europe's large, integrated chemical/pharmaceutical companies have assimilated this new technology over the last decade.

Simon Shackley has been a graduate student at SPRU from 1987 to 1991 taking first the MSc in Science, Technology and Innovation Studies, and subsequently continuing as a doctoral student under Margaret Sharp. He has recently submitted his D.Phil entitled *Regulating the New Biotechnologies in Europe*. This was concerned with describing, analysing and evaluating regulation for the new biotechnologies in the UK, France, Germany, Denmark and the EC.

2. *How and why is biotechnology important to the UK industry*

Biotechnology is an important enabling technology, or, strictly speaking a series of enabling technologies. (In this sense the French—les biotechnologies—is more satisfactory than the English biotechnology.) In pharmaceuticals it is now an essential part of drug discovery mechanisms enabling researchers to discard the traditional route of (relatively) random screening for new chemical elements (NCEs) of therapeutic value in favour of a more targeted and "rational" approach based on a better understanding of the body's own biochemistry and immune response mechanisms. In agricultural biotechnology, it likewise builds on detailed knowledge of plant metabolism. In both sectors, biotechnology now provides the leading edge of technology. Any company which wishes to remain competitive in world markets in either of these two areas has to take this new technology on board.

3. *What future prospects and opportunities does the technology offer?*

As is well known biotechnology has widespread application to the chemical and pharmaceutical industries and in the development of medical and animal sciences. The most advanced area of development is that of pharmaceuticals and human and animal healthcare where new biopharmaceutical drugs and vaccines are now being launched on the market and where gene therapy offers a wholly new approach to disease control. After pharmaceuticals, agricultural applications are the most advanced, in particular the development of transgenic plant species which offer the possibility of helping solve the world food problem by breeding plants resistant to disease and capable of overcoming climatic and soil disadvantage.

In the long run, the agricultural applications hold out the potential for another green revolution, raising productivity and living standards in many of the poor agricultural areas of the world. In the shorter run many of the techniques of "second generation" biotechnology, eg tissue culture, biomass energy, offer ways of raising living standards which are relatively cheap and can build on local skills. They also avoid the problems of patenting, etc., which currently inhibit the use of many third generation techniques in Third World countries. Other applications are in the food industry where developments make it possible to synthesize artificially naturally occurring sweeteners/flavours ranging from sugar to coffee. Developments in biotransformations hold out the possibility of substantial application in the chemical industry, particularly in fine chemicals, but at present this is little advanced. There are also major applications to be exploited in waste management and pollution control, but this requires a public sector lead which has so far been lacking.

4. *Which developments in biotechnology raise issues of safety and how should they be addressed*

In so far as the technology is involved in producing medical and food products and/or the releasing of genetically modified microbes into the environment, there are issues involving health, safety and/or potential environmental hazards. The development of new drug therapies need to satisfy the normal safety standards laid down by both the British and EC authorities. The use of genetic engineering techniques in the development of these drugs, and the possible release into the environment of genetically modified organisms (GMOs) pose different problems and because there was no prior history of such releases the risks were, and to a degree remain, unquantifiable. Initially there were fears that any such release might open a Pandora's box involving the proliferation of mutant species in the environment. For this reason, early experiments took great care to maintain strict controls, using the highest categories of security in laboratory experiments and monitoring all outcomes very carefully. As time has gone by, these experiments have shown that there is little risk to health or safety provided good laboratory practice is adhered to. The main concern and focus of attention today surrounds the release into the environment of GMOs where, although the experiments to date indicate little danger of major disasters, we still do not know what the longer term effects on the ecosystem will be. This is why we still need to proceed cautiously, with carefully controlled, monitored experiments—a step by step learning process.

The following grid illustrates the different safety aspects of the different types of release. It distinguishes between risks to human health and safety which arise in work from risks which arise from consumption or use by consumers. The numbers in the grid relate to the notes below. These notes are no more then summaries of the main issues involved and it is really necessary to ask the experts involved to flesh out the details. (Neither of us would claim to be experts.)

	Safety Aspect		
Application	*Occupational H&S*	*Environmental Risks*	*Product Risks*
Contained use of GMOs			
(a) research	*i*	*ii*	
(b) pilot	*iii*	*iv*	
(c) production	*v*	*vi*	
Deliberate release of GMOs			
(a) R&D	*vii*	*viii*	
(b) commercial	*ix*	*x*	*xi*
Product Use & Consumption			
(a) foods		*xii*	*xiii*
(b) drugs		*xiv*	*xv*
(c) misc		*xvi*	*xvii*

i and iii There are known risks even in research which are controlled by fairly long established protective measures and practices (both hardware and software, such as training). Even now, however, the risk assessment is only semi-quantitiative and the implementation of the regulations are unclear, except perhaps to the HSE Inspectorate. There are also potential risks, some very serious (e.g. in oncogenic research) which are also controlled by precautions. The case of the deaths at the Pasteur Institute of those engaged in oncogenic research are a timely reminder that biological research can be very dangerous.

ii and iv There are risks mainly arising from (and probably better dealt with by treating) emissions. But in practice these are not always recognised and there is too much sloppy practice e.g. in washing laboratory equipment.

v The risk issues for production are different even though the strategies for protection against them are similar to (i). The immunogenic response of workers to exposure to biological agents and products is particularly important.

vi There is precious little risk assessment research on this issue and some evidence that industry does not recognise how important it is.

vii There might be specific risks of immunogenicity.

viii The risks are largely potential and it is very difficult indeed to say in general terms what the greatest possible risks are or the probability of their arising. In other words we are a long way from being able to quantify this. One route is to distinguish in a rough fashion between types of genetic modification and ecosystems on the lines suggested by the Ecological Society of America. The Royal Commission on Environmental Protection (RCEP) GENHAZ scheme with its cautious case by case, step by step approach has considerable merit.

x The environmental risks of commercial use are less controllable than in R&D (viii above). Some sort of post-marketing surveillance of newly introduced GHOs, rather on the same lines as happens with new pharmaceuticals, might be a useful way to proceed. There are likely to be some ecological surprises in store when GHOs are released commercially; we must learn as much as possible from these.

xii Food safety and nutritional issues (toxicity, antigenicity, etc) are raised by consuming products produced by and/or consisting of or containing GHOs.

xiii If foods contain live GHOs it could raise some environmental issues.

xiv The usual issues of safety, quality and efficacy of drugs and biologicals are raised, although there might also be issues specific to GMO-derived products. (e.g. the presence in the product of introduced DNA).

xv If drugs contain live GHOs environmental issues are raised. e.g. live, genetically modified vaccines could have a range of potential effects on a number of organs.

xvi GHOs might be sold as garden plants with possible health and environmental effects—or for that matter such things as sunflower seeds for birds might come from genetically manipulated plants.

5. *Should biotechnology be regulated by an industry specific regime?*

If by "industry specific regime" you mean specific to biotechnology the answer is "yes". For the reasons stated in (4) above, we believe that it is right for the present to have a special regime applicable to products which are in one way or another "transgenic". Such a regime needs to be well integrated into, and coordinated with, other regulatory systems aimed at protecting health, safety and the environment. There will inevitably remain some aspects—eg the safety, efficacy and quality of food, drugs, new crops, pesticides, etc,—which have to be dealt with by other agencies.

6. *Horizontal versus vertical regulation*

We find this question confusing. In the first place all regulation for occupational health and safety is *of its nature* process based. It is also quite common for regulation to be both product and process based—for example the regulation of pharmaceuticals looks both to the safety of the product and to the cleanliness etc of the production processes by which it is produced. Moreover much regulation—eg that on the environmental release of GMOs—would require one set of regulations on environmental risks and other regulations on other aspects. (See the grid in question 5 above.)

What we suspect this question is getting at is whether a product that has been produced by some form of genetic modification (eg the Flavr Savr tomato) should be treated in any way as exceptional. Our answer, as implied in our answer to question 5, is that we think that for the present this "exceptionalism" should remain. We recognise that such an approach is taking environmental protection to a new level of precautionary care, but this is seen as a good thing by many commentators and in our view this is right *given the present state of knowledge*. This type of precautionary approach is what has distinguished the regulation of genetic engineering since that technique was invented 20 years ago and compares favourably with many other areas of regulation (cf food additives, pesticides, water quality). It is not seen as excessive when applied to research or production (see our answer to question 4 above). Given the harm that has been done in the past to the environment because of thoughtless releases of hazardous substances, we believe that in this instance the precautionary approach is both right and appropriate.

7. *From horizontal to vertical control?*

We believe that once there is sufficient evidence upon which to base judgement (as has happened with contained use experiments where the levels of safety precaution have been substantially relaxed) that it is right, provided there is no evidence of detrimental effect, to drop the precautionary approach. The problem, however, is what criteria should be used in making such judgements. Administratively it might make sense, as experience develops, to regulate products in sectoral divisions—eg agriculture, food, drugs, etc—but this is not necessarily efficient because it would still require the sectoral divisions to monitor ecological questions and/or to have their own specialist committees and experts on these issues. This is why it probably makes more sense to continue with a forum, such as the Advisory Committee on Releases into the Environment (ACRE) where specialist expertise on the ecological issues resides and can develop.

8. *Comparisons in regulation between the UK and competitor countries*

Europe

In theory much regulation of the new biotechnologies is harmonised across the EC with the passing of the three directives on (i) contained use (90/219), (ii) deliberate release (90/220), and (iii) protection of workers (90/679). In addition other directives which regulate the development and use of certain categories of GMO (eg plant protection products, novel foods) have been, or are in the process of being, formulated and implemented. There is, however, still a good deal of ambiguity and there remains considerable uncertainty as to how some categories of GMO will eventually be regulated.

While regulation has been harmonised, implementation rests with individual member states and there is very considerable variation both in terms of coverage and interpretation from country to country. The legal basis of the Directives is important in this respect. For example, the contained use directive allows member states to impose more stringent controls if they wish, whereas the deliberate release directive prevents this but requires a high level of protection. The position of the regulatory agencies and advisory committees *vis a vis* the different types of risk is one factor influencing the way in which the directives are implemented. In the past, the authorities in Germany and Denmark have taken a more cautious approach towards health and environmental risks than their counterparts in the UK and France and there is therefore rather more criticism from these latter countries of the delibrate release directive than from the former.
Recent reports, however, indicate that scientists and industrialists in Germany are finding the 1990 German Gene Law (which imposes rather tighter controls than the EC directives)too stringent and are calling for its revision. Different national approaches towards regulation reflect, in part, different attitudes on the part of the population towards the risks involves. The EC Concertation Unit's (CUBE) Euro-Barometer survey of public concern about the new biotechnologies indicated very considerable variation from country to country.

The ambiguity of the directives and the requirement that detailed implementation is to be at member state level creates much potential for variations in interpretation. For example, decisions about inspection and consultation (e.g. who is to be consulted in the case of a deliberate release) are left largely to national authorities and yet can be critical factors in the success and acceptance of regulation. The almost total absence of any prior system of regulaton in many of the Southern member states also creates difficulties since most of them have neither the knowledge nor the capability to implement the directives. The Article 21 Committees established by 90/219 and 90/220 are supposed over time to harmonise the regulatory assessment criteria. This will clearly require detailed negotiations between national regulatory authorities and will be both a learning process in itself and provide an important forum for those without prior experience to learn from their counterparts in other countries.

It is worth noting that the regulation of existing (second generation) biotechnologies is less harmonised across the EC than the control of GMOs and for most countries there are "gaps" in the treatment and recognition of biological risk.

The United States and Japan

We do not have detailed knowledge of the regulatory frameworks in these countries and would defer to those who are more expert in these matters. In general, the perception is that in both these countries regulations, particularly in respect of deliberate release, are less demanding than in the EC. Under Vice President Dan Quayle, the White House strongly advocated regulation of GMOs on a sectoral basis, a position supported by some agencies including the FDA, but not by others including the EPA. The policy is now seen by some commentators to have back-fired, alienating not only environmental and consumer groups but some companies, and it is likely to be changed under the Clinton Administration.

9. *The consequences of the regulatory regime on competitiveness of UK industry*

There is very little clear evidence about the effects of regulation on competitiveness. It tends to be assumed that the tougher the regulatory climate, the more difficult it is for firms based on that area to compete with those not facing such regulations, but this is not necessarily so. For example, with pharmaceuticals the US regulations have long been regarded as being the toughest in the world, yet the US industry is also regarded as the most competitive in the world. Within Europe, the British pharmaceutical industry has emerged over the last 20 years as a major global competitor partly because its tougher stance on pharmaceutical safety and efficacy (than say the French industry) has discouraged the development of "me-too" pharmaceuticals and encouraged the growth of an innovative drug industry. Likewise, while Germany has the toughest anti-pollution laws on electricity generation, its industry has benefited from being first in the field in the development of new equipment. In all these cases, it is necessary to look beyond the immediate effects of regulation on sales to its longer term impact on innovation.

It is also important to recognise that many of the leading companies in the sectors most immediately involved in biotechnology are major multi-nationals with R&D facilities in more than one country. If regulations inhibit research in one country it is therefore relatively easy for such companies to switch research to another country with a more "conducive" regulatory climate. For example, it is widely claimed that the German pharmaceutical/chemical companies have switched much of their biotechnological research to their US-based facilities in order to avoid the more restrictive attitudes towards this research in Germany. Even if this is the case the companies remain German-based companies and *their* competitiveness benefits.

However, in our view the case that these companies have shifted research off-shore *just because of the tougher regulatory climate* remains unproven. Important other factors have also influenced developments. One such factor is that these companies have been simultaneously trying to develop their market base in the US and were expanding by merger and acquisition which often brought good research laboratories with them. (For example, Bayer's acquisition of Miles brought them the New Haven laboratories which they have now expanded considerably to be their main pharmaceutical base in the US.) Moreover, the attraction of the US was *not just* the more liberal regulatory climate. Another major attraction was undoubtedly the quality of the research base in biotechnology in the US and its accessibility via US universities and the new biotechnology companies. A further factor favouring the US has been the *certainty* of its regulatory regime. For Swiss and German firms, the long uncertainty as to precisely what type of regime would emerge inhibited long term investments.

In this context, it is interesting that UK companies have been much less active in forming alliances with US partners than their German or Swiss counterparts. Depending upon which way you look at it, this could either reflect the more liberal regulatory regime in the UK than in Germany or Switzerland, the higher quality of the science base in this area in the UK, or the risk averse strategies of UK multinationals—or, of course, a little bit of all three. It nevertheless serves to illustrate how complex are the issues underlying competitiveness and how regulation is but one part in a complex jigsaw.

The most undesirable aspect of the current situation is the degree to which differences in regulation are becoming weapons of mercantilism, with the more liberal regime of the US (and on the patenting issues) seemingly being used as a competitive tool for attracting high value added jobs to the US. Given that environmental factors are no respecters of national frontiers, there is a strong case for setting generally agreed international standards for both regulation and IPR—in effect for creating an international level playing field.

This said, in so far as the current EC regime is tougher than that in the US and Japan, then the shorter term effects could be expected to be as follows:

(i) *research*—not much affected; most research is undertaken in contained use facilities and OECD guidelines on good industrial practice are adhered to; (but see answer to Question 10 below.)

(ii) *product development*—the main problem arises for any product that needs to be tested outside contained facilities—eg transgenic plant species. Tougher regulations add to development costs.

(iii) *investment*—as (ii) above.

(iv) *location*—as indicated above, it might influence multinationals to take R&D and investment overseas, but there are other factors at play besides regulation.

(v) *sales and marketing*—there seems little problem with the marketing of drugs which have been derived via genetic manipulation, but there is a problem in relation to seeds, plants and foodstuffs where marketing raises all the issues of labelling mentioned above.

10. *Will the present regulatory regime prevent the exploitation by British industry of British research?*

The problem only arises in relation to environmental release, not in relation to contained use facilities (eg in drug development). Here one of the main problems arises in relation to research at British universities and to a lesser extent at research council institutes. Very few releases have taken place to date at universities, and it would appear that one of the main reasons is the lack of resources necessary to meet the regulatory requirements. The answer might be for universities/institutes to combine together to share the costs involved, or to work in cooperation with companies. Research councils and other funders must accept that they need to provide enough funds to cover this dimension.

11. *How can the issues of public acceptance best be addressed?*

We believe that the issues of public acceptance can best be addressed by the industry taking the public into its confidence, explaining what it is doing, making experiments and subsequent data open to public scrutiny and generally being open and above board in all actions. The logic of this stance argues:

(a) for more representation on scrutiny committees of lay people, ecologists, etc (their exclusion merely exacerbates fears);

(b) for open labelling of products which are the result of experiments (eg, of genetically manipulated tomatoes). The challenge for companies is to try to make the label *This product is from a genetically modified plant* a positive rather than a negative for the consumer. The danger of not having labels is a consumer backlash when it is revealed that some foods are based on GMOs.

There is also a case for setting up an experimental Public Commission on Biotechnology consisting of a range of lay persons as well as experts. In both Germany and Denmark such Commissions seem to have worked well in helping the public understand the issues involved with biotechnology, and not just the health and safety issues, but the social, moral and economic issues as well. Some people are more worried by the latter than by the former, but at present there is no real outlet for discussion of their fears.

12. *Other factors playing a crucial role in the competitiveness of UK biotechnology*

We list below some of the factors which in our opinion will play an important part—indeed a more important part than any of the regulatory factors—in the development of biotechnology in the UK. It is also worth noting that the past regulation of rDNA work (contained use and deliberate release) in the UK has in fact helped to create a positive "climate" for such work and associated investments in the UK compared to countries such as Germany.

(a) *Quality of the science base*—access to leading edge research is undoubtedly the most important factor influencing the local and corporate R&D facilities;

(b) *Readiness of UK companies to exploit that science base*—there is anecdotal evidence indicating that UK industry is less willing than its counterparts to exploit the science base in this country. This is put down variously to the dominance of short termism in Britain (with more attention being paid to divdend payments and share price than in any other country); lack of competition, particularly from the small firm sector (wheras in the US the multinational chemical/pharmaceutical companies are constantly being channelled by their small firm competitors) (see (c) below); and the lack of understanding of the technology and its implications by the management cadre in these firms;

(c) *Availability of venture capital and "exit route" for investments*—the UK and Europe generally hosts a small number of new firms than might be expected given its strength in the pharmaceutical and chemical industries. One of the main reasons for this is the limited nature of the venture capital market which in turn is affected by the lack of an "exit route" for shareholders (ie, the inability to sell shares on stock market as in US NASDAQ system).

Evidence from J F Thorley

1. *Interest in Biotechnology*

Today the writer's interest in Biotechnology is that of a consultant. He has, however, spent a full professional career in large scale Biotechnology as a member of the pharmaceutical industry. This career culminated in being the European Technical Advisor for Eli Lilly and Company.

He is a long-standing member of the CBI Working Party and previously of the biotechnology committees of other trade associations, a member of ACGM and previously GMAG, a consultant on GILSP to OECD and a consultant to the European Commission and United Nations.

Unfortunately the writer was in the USA on the date when the CBI gave oral evidence to the House of Lords. Normally he would have been part of the delegation.

2. *Evidence*

The evidence which is to be offered addresses Questions 2, 3, 4, 5, 6 and 7 on the invitation paper suggested by the House of Lords. The evidence is based on a large scale survey which the writer is undertaking for the European Commission on the amplification of the Engineering concept of Good Industrial Large Scale Practice in Biotechnology. The comments are based on an in-depth study of some 12 major industry sectors which currently use biotechnology. These range from vaccine manufacture to waste treatment.

The feeding of Europe is the largest single occupation of the European labour force; it is also the most important industry. Biotechnology has traditionally been used in many ways for food and drink production using safe, non-recombinant, but strain selected, micro-organisms and in the future must turn to the use of safe recombinants in order to remain competitive with other major trade areas, the USA and the Pacific Rim.

The food and drink industry rightly recognises the considerable public perception problems which may accompany the introduction of recombinants and has wisely stayed quiet on the subject during recent years. In the period the pharmaceutical industry has taken an early leading role.

These recent years have, however, seen a considerable focusing on additional biotechnology regulations, which have been taken in conjunction with a recent upsurge in environmental considerations and regulations. It is, therefore, perhaps unfortunate that those few industry views which have been expressed have been largely those of only the pharmaceutical industry, which has the advantage that the new drugs created using recombinant DNA techniques usually have life saving properties and hence an enhanced public perception. The views of this industry are not necessarily representative of the whole range of industries which use biotechnology.

Much of the current national legislation of EC member states and directive 90/219/EEC on the contained use of micro-organisms is based upon the original work of the OECD, which culminated in the issue in 1986 of the "Blue Book"—RDNA Safety Considerations. The committee responsible for this work, of which the writer was a member, was largely made up from governmental officials with only five industrialists, all of whom were from the pharmaceutical industry. The written considerations, which are probably the most balanced comments on biotechnology, formally introduced the concept of good industrial large scale practice for the first time and also suggested containment measures for organisms which did not fall within this category.

These containment measures were originally meant purely as examples. For safe GILSP organisms OECD was clear that existing safe industrial practices would be sufficient, adapted where necessary to incorporate modern concepts of occupational hygiene and safety.

In the absence of other information from industry too much has become associated with these examples of containment, which have become incorporated into later legislation and furthermore have, in the eyes of many, been assumed to have some form of connection with the requirements of GILSP. This is in practice reasonable in the case of the pharmaceutical industry but not for other industries.

Unfortunately for various reasons OECD did not have the opportunity to amplify in practical engineering terms its concept of GILSP as applied to other industries and this resulted in the original recommendations becoming used as the basis for this European Directive, which additionally incorporated a large number of risk assessment and reporting measures by users and a large centralised bureaucratic approval and reporting system to be carried out by national competent authorities and the EC. All of this was based on the assumption that the original OECD recommendations could be taken and applied in a meaningful manner across a whole set of pan industry sectors and administered with equal validity by a centralised Environment/Health and Safety bureaucracy at national and EC levels.

The purpose of the study which the writer has been undertaking has been to examine in detail:

(a) what constitutes existing good industrial practice in all the major industry sectors which use biotechnology.

(b) to compare these practices in order to examine the nature and magnitude of any practical commonalities.

(c) to recommend ways in which the legislation and its administration might be modified to take care of the real industrial systems rather than continue to use the model, based on the pharmaceutical industry, which has become associated with the legislation.

The survey has illustrated the following points:

(A) There are no examples in the very important food and drink sectors of these industries using other than safe organisms.

(B) The consideration given to the use of dangerous organisms has been given far too much prominence in both the directives and all the technical discussions which have surrounded the legislation in the last few years. The only area in which pathogens are used at large scale in the pharmaceutical industry and then only for a very small part of its total output.

It is accepted that the handling and the discharge of pathogenic organisms, be they traditional or recombinant, must be treated with great care because of the potential for harm but it must be recognised that the industry has used these organisms at various degrees of large scale for most of the present century without accident.

(C) The study has shown that existing good practice in the use of safe traditional organisms varies enormously from industry sector to sector and also that there often is, in the traditional industries, considerable variation within the sectors.

This means that for the concept of good large scale practice to have any real meaning and to be used as the basis for realistic risk assessments, it must be developed on an industry basis not in a vacuum by legislators, EC or National, but by joint Industry Expert/Legislator groups. Only then will the concepts have any useful meaning by which individual applications to an enforcement agency can be judged in a fair and reasonable manner.

(D) There is in fact no such thing as a single "Good Large Scale Practice" operable across all industry sectors but a series of good large scale practices, only operable and fully understood by the industry for which they were developed.

(E) If it is accepted that good industrial practice for the use of safe micro-organisms, traditional and recombinant, is an industry specific concept, then the idea of pan industry sector horizontal legislation ceases to have any validity and with it the need for a centralised enforcement agency either in environment or health and safety.

Control and, where necessary, enforcement, should more properly be associated with government departments more normally responsible for the activities of a particular industry sector such as DOH, MAFF, DTI in the UK and DG 3 within the European Community.

(F) In the view of the writer there is an urgent need to completely re-evaluate the new UK legislation, including section 6 of the Environmental Protection Act and to apply the concept of deregulation to this legislation in the context of fulfilling the requirements of the EC directives as they presently stand but also to see what opportunities deregulation would bring, coupled to a similar exercise applied to the European Directives.

(G) It is recommended that the UK government takes very positive steps to ensure that the existing EC directives are completely overhauled on an industry specific basis and that the appropriate sponsoring Directorates are chosen within the Commission to implement this work.

(H) The acceptance of the products of Biotechnology and of its new techniques is extremely dependent on the public perception of both the products and, in today's age, of the way in which they are made.

Although industry can contribute to this public acceptance, it is perceived and probably correctly as only promoting its own products. There is therefore an urgent need for a transparent, continuous, positive public perception role in government to support UK industry.

In addition the government should also urgently encourage the EC to have a community wide public perception programme. Biotechnology and its operating companies are today European and world-wide.

Supplementary Evidence from the EC Commission

Question 1

What was the origin of the two Directives concerning the use and release of genetically modified organisms 90/219 and 90/220?

The origin of the Directives is best explained by the events which led up to their being proposed in 1988.

Since the Asilomar Conference (February 1975) the regulation of biotechnology has attracted public and political interest. In 1978 the Commission proposed a Directive on containment standards. Following this proposal in 1982 the Council adopted a recommendation (1982/472/EEC) concerning the registration of work involving rDNA. It stated that national authorities should maintain registries of rDNA work. In its 1983 communication (COM/83/672) the Commission had emphasised the regulatory aspect not only to anticipate the commercial innovations from biotechnology but to create harmonised conditions for a Common Market. In particular, the Commission made clear (p. 11) that it would put forward general or specific proposals appropriate to create a regulatory framework suitable for the development of the activities of the bioindustries and for the free circulation of goods produced by biotecnology.

In 1985, the Commission started to assess further the need for Community legislation in the area of biotechnology. Existing Community legislation at that time in respect of products, worker protection and environmental protection was being revaluated as to its adequacy. In April 1986, a high level meeting with Member States officials to discuss the regulation of biotechnology within the Community took place, based on the OECD report on rDNA safety considerations.

Moreover the Commission consulted with the industries most involved in modern biotechnology, which submitted a joint report to the Commission setting out their views on the need for Community wide regulation of biotechnology.

In November 1986 the Commission issued a Communication to the Council (COM/86/573) on a Community framework for the regulation of biotechnology. In this Communication (page 4) the commission stated the following:

> "In the light of the examination which the Commisssion undertook, it believed that the rapid elaboration of a Community framework of biotechnology regulation to be of crucial importance for the industrialisation of this technology in the Community. Equally citizens, industrial workers, and the environment need to be provided with adequate protection throughout the community from any potential hazards arising from the application of these technologies. The internal market arguments for Community wide regulation of biotechnology are clear. Microorganisms are no respecters of national frontiers, and nothing short of Community wide regulation can offer the necessary consumer and environmental protection".

In this 1986 Communication it therefore announced that proposals for biotecnology legislation would be introduced. Subsequently, after a number of consultations with outside experts in 1988 the Commission submitted proposals to the Council for three Directives: (COM/88/160, COM/88/165); on the contained use of genetically modified microorganisms; on the deliberate release into the environment of genetically modified organisms and on the protection of workers from the risks related to exposure to biological agents at work. These proposals were adopted after modification by the Council as Directives 90/219/EEC, 90/220/EEC and 90/679/EEC.

This historical overview shows that the Directives were put forward after a careful examination by the Commission lasting quite a number of years.

Question 2

What were the criteria used to draw up the Directives?

The two main guiding principles were:

- the precautionary principle as part of the health, safety and environmental policy of the Community.
- the objective of harmonising the laws of the Member States in order to permit the proper functioning of the internal market for biotechnology.

The scientific and technical criteria were drawn from the 1986 OECD Council recommendation "Concerning Safety Considerations for Applications of recombinant DNA organisms in Industry, Agriculture and the Environment". It served as a reference point.

Question 3

Who were the experts consulted by the Commission about the Directives?

In preparing the draft proposals for Directives 90/219 and 90/220, the Commission consulted Member State experts and Industry organisations as well as individual companies. The industry associations consulted both before and after the proposals were published were ECRAB (European Committee on the Regulatory Aspects of Biotechnology—whose secretariat was EFPIA) and subsequently EBCG (European Biotechnology Coordination Group—whose members were AMFEP, CEFIC, CIAA, EFPIA, GIFAP).

Question 4

What is the EC doing to examine the situation in order to produce a "level playing field" for biotechnology?

At present, 1½ years after the two Directives came into force, all the Member states have appointed Competent authorities to deal with the applicants and have set up the necessary administrative systems. In three Member States the implementing legislation is still under discussion (Greece, Luxembourg and Spain) and it is expected that the process will be completed shortly. The Commission has written to a number of Member States, commenting on their transposing legislation, where the Commission considers it to be incomplete, incorrect or over zealous.

The Commission will give more details on the implementation of the Directives in 1993 in the reports as demanded by Article 22 paragraph 3 of Directive 90/220/EEC, and by Article 18 paragraph 3 of Directive 90/219/EEC.

Question 5

What are the possibilities for simplification for the UK under directive 90/220/EEC and how quickly will the Commission move on simplification?

Directive 90/220/EEC contains several possibilities for the Directive to be simplified without amendment.

Under Article 5 (3) the competent authorities may accept that releases of a combination of GMOs on the same site or of the same GMO on different sites for the same purpose and within a limited period may be notified in a single notification.

Article 20 permits the Commission, via the procedure laid down in article 21, to adapt Annexes II and III in order to take account of scientific and technical progress.

Article 6 (5) provides the possibility for the application of simplified procedures to be requested by the Competent Authority for releases of certain GMOs for which the Competent Authority considers that sufficient release experience has been gained. Under this Article, the Competent Authorities of France, Belgium and the UK have submitted proposals for simplification taking account of the experiences obtained from certain types of GMO. At present the Commission is drawing up appropriate criteria in order to take a decision on each of the applications. Consultations on this proposal have taken place with four European Industrial Associations GIBIP, ESNBA, COMASSO and SAGB, as well as with the academic community and Member State experts. The criteria shall be based on safety to human health and the environment, and on the evidence available on such safety. The Commission aims to adopt the decision, which will be taken via the prcedure as laid down in article 21, shortly.

Question 6

The interim report on the regulatory framework on biotechnology in the EC and USA does not seem to draw any conclusions on the merits of the respective systems?

The Commission started a fact-finding exercise focusing in the first instance on a comparison of EC and US regulations on plants, micro-organisms, microbial pesticides and research policy. An interim report was published containing the first results of this work. The report made a number of preliminary findings which will be finalised after comments from interest groups have been received. The preliminary findings indicate that:

- the differences between the EC and US at the pre-marketing stage are that in the US the scope is different and that within that defined scope, there exists more flexibility. However, at the present stage of development of biotechnology, practical experience indicates that most field releases carried out in the EC and US were covered by the respective regulatory frameworks. There is also a similarity in the method and information requirements for a risk assessment of a release to the environment.
- At the marketing stage, the major difference identified is that in the US there is no equivalent to the EC's one notification—one authorisation procedure once such produce leglislation is in force in the EC.

Question 7

What other EC legislation is in the pipeline?

The Commission has proposed or is at present preparing new, and changes to existing, product legislation in order to provide for a specific environmental risk assessment similar to that laid down in Directive 90/220/EEC before the placement of products containing GMOs on the market.

Such product legislation will come into force shortly for medicinal products. A similar proposal for noval foodstuffs in under discussion with the European Parliament and the Council. As far as pesticides and plant seeds are concerned such leglisation is under preparation within the Commission.

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